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A TEXT-BOOK
OF
HUMAN PHYSIOLOGY

BRUBAKER

A TEXT-BOOK
OF
HUMAN PHYSIOLOGY
INCLUDING A SECTION ON
PHYSIOLOGIC APPARATUS

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FIFTH EDITION. REVISED AND ENLARGED

WITH 1 COLORED PLATE AND 359 ILLUSTRATIONS

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TO

KENNETH M. BLAKISTON

LOYAL FRIEND COURTEOUS GENTLEMAN
GENEROUS PUBLISHER
THE PRESENT EDITION OF THIS WORK
IS
AFFECTIONATELY DEDICATED

PREFACE TO FIFTH EDITION

In the preparation of the fifth edition of the Text-book of Physiology the attempt has been made once again to increase its value to those for whom it is primarily intended, viz., students of medicine and practitioners who desire to keep in touch with the progress of physiology. With this view the text has been subjected to careful revision and in many sections entirely rewritten. Some of the anatomic diagrams have been eliminated and physiologic diagrams inserted. The suggestions and criticisms contained in reviews and book notices, in letters from teachers and practitioners have been considered and in many instances adopted, with benefit to the text, for all of which the writer expresses his appreciation.

Among the subjects which have been added, enlarged or revised may be mentioned the metabolism of the food principles; carbohydrate metabolism; the electric currents of the heart and their graphic registration, the electro-cardiogram; animal heat; internal secretion; the localization of functions in the cerebral cortex; the autonomic nerve system, etc. These changes have necessitated the elimination of less important material, but, nevertheless, some thirty-seven additional pages have been added to the general body of the text.

To those teachers and students who have recommended and used this work and to whom I am indebted for generous praise, kind criticisms, and helpful suggestions, I wish to express my sincere thanks and trust that in its improved form it will continue to meet their approval.

Once again I desire to express my appreciation of the unwearied and invaluable assistance of Mr. I. A. Hagy in preparing the manuscript for the press.

To Messrs. P. Blakiston's Son & Co. I am greatly indebted for their encouragement and generosity in the promotion of everything that pertains to the material value of this work.

A. P. B.

PREFACE TO FIRST EDITION.

The object in view in the preparation of this volume was the selection and presentation of the more important facts of physiology, in a form which it is believed will be helpful to students and to practitioners of medicine. Inasmuch as the majority of students in a medical college are preparing for the practical duties of professional life, such facts have been selected as will not only elucidate the normal functions of the tissues and organs of the body, but which will be of assistance in understanding their abnormal manifestations as they present themselves in hospital and private work. Both in the selection of facts and in the method of presentation the author has been guided by an experience gained during twenty years of active teaching.

The description of physiologic apparatus and the methods of investigation, other than those having a clinical interest, have been largely excluded from the text, for the reason that both are more appropriately considered in works devoted to laboratory methods and laboratory instruction, and for the further reason that the student receives this information while engaged in the practical study of physiology in the laboratory, now an established feature in the curriculum of the majority of medical colleges. For those who have not had laboratory opportunities a brief account of some essential forms of apparatus and the purposes for which they are intended will be found in an appendix.

I wish to acknowledge my indebtedness to Professor Colin C. Stewart for many valuable suggestions in the preparation of different sections of the volume; to Dr. Carl Weiland for assistance in the chapter on vision; to Dr. Joseph P. Bolton for excellent suggestions on questions relating to physiologic chemistry.

TABLE OF CONTENTS.

PAGE

CHAPTER I.

INTRODUCTION 1

CHAPTER II.

CHEMIC COMPOSITION OF THE HUMAN BODY 6

CHAPTER III.

PHYSIOLOGY OF THE CELL 24

CHAPTER IV.

HISTOLOGY OF THE EPITHELIAL AND CONNECTIVE TISSUES 31

CHAPTER V.

THE PHYSIOLOGY OF MOVEMENT 39

CHAPTER VI.

THE PHYSIOLOGY OF THE SKELETON 47

CHAPTER VII.

GENERAL PHYSIOLOGY OF MUSCLE-TISSUE 51

CHAPTER VIII.

THE GENERAL PHYSIOLOGY OF NERVE-TISSUE 90

CHAPTER IX.

FOODS 116

CHAPTER X.

DIGESTION 136

CHAPTER XI.

ABSORPTION 210

CHAPTER XII.

THE BLOOD 230

CHAPTER XIII.

THE CIRCULATION OF THE BLOOD 264

CHAPTER XIV.

THE CIRCULATION OF THE BLOOD (Continued) 328

Page

CHAPTER XV.

Respiration 377

CHAPTER XVI.

Animal Heat 438

CHAPTER XVII.

Excretion 453

CHAPTER XVIII.

External Secretions 476

CHAPTER XIX.

Internal Secretion 490

CHAPTER XX

Metabolism 509

CHAPTER XXI.

The Central and Peripheral Organs of the Nerve System 523

CHAPTER XXII.

The Medulla Oblongata; the Isthmus of the Encephalon; the Basal Ganglia . . 551

CHAPTER XXIII.

The Cerebrum 570

CHAPTER XXIV.

The Cerebellum 603

CHAPTER XXV.

The Cranial Nerves 610

CHAPTER XXVI.

The Autonomic Nerve System 640

CHAPTER XXVII.

Phonation; Articulate Speech 658

CHAPTER XXVIII.

The Senses of Touch, Taste and Smell 669

CHAPTER XXIX.

The Sense of Sight 679

CHAPTER XXX.

The Sense of Hearing 713

CHAPTER XXXI.

Reproduction 726

APPENDIX.

Physiologic Apparatus 741

Index 767

TEXT-BOOK OF PHYSIOLOGY

CHAPTER I

INTRODUCTION

An animal organism in the living condition exhibits a series of phenomena which relate to growth, movement, mentality, and reproduction. During the period preceding birth, as well as during the period included between birth and adult life, the individual grows in size and complexity from the introduction and assimilation of material from without. Throughout its life the animal exhibits a series of movements, in virtue of which it not only changes the relation of one part of its body to another, but also changes its position relatively to its environment. If, in the execution of these movements, the parts are directed to the overcoming of opposing forces, such as gravity, friction, cohesion, elasticity, etc., the animal may be said to be doing work. The result of normal growth is the attainment of a physical development that will enable the animal, and, more especially, man, to perform the work necessitated by the nature of its environment and the character of its organization. In man, and probably in lower animals as well, mentality manifests itself as intellect, feeling, and volition. At a definite period in the life of the animal it reproduces itself, in consequence of which the species to which it belongs is perpetuated.

The study of the phenomena of growth, movement, mentality, and reproduction constitutes the science of **animal physiology.** But as these general activities are the resultant of and dependent on the special activities of the individual structures of which an animal body is composed, **physiology** in its more restricted and generally accepted sense is the science which investigates the actions or functions of the individual organs and tissues of the body and the physical and chemic conditions which underlie and determine them.

This may naturally be divided into:

1. *Individual physiology*, the object of which is a study of the vital phenomena or functions exhibited by the organs of any individual animal.
2. *Comparative physiology*, the object of which is a comparison of the vital phenomena or functions exhibited by the organs of two or more animals of different species, with a view to unfolding their points of resemblance or dissimilarity.

Human physiology is that department of physiologic science which has for its object the study of the functions of the organs and tissues of the human body in a state of health.

Inasmuch as the study of function, or physiology, is associated with and dependent on a knowledge of structure, or anatomy, it is essential that the student should have a general acquaintance not only with the structure of man, but with that of typical forms of lower animal life as well.

If the body of any animal be dissected, it will be found to be composed of a number of well-defined structures, such as heart, lungs, stomach, brain, eye, etc., to which the term organ was originally applied, for the reason that they were supposed to be instruments capable of performing some important act or function in the general activities of the body. Though the term organ is usually employed to designate the larger and more familiar structures just mentioned, it is equally applicable to a large number of other structures which, though possibly less obvious, are equally important in maintaining the life of the individual—*e.g.*, bones, muscles, nerves, skin, teeth, glands, blood-vessels, etc. Indeed, any complexly organized structure capable of performing a given function may be described as an organ. A description of the various organs which make up the body of an animal, their external form, their internal arrangement, their relations to one another, constitutes the science of **animal anatomy.**

This may naturally be divided into:

1. *Individual anatomy*, the object of which is the investigation of the construction, form, and arrangement of the organs of any individual animal.
2. *Comparative anatomy*, the object of which is a comparison of the organs of two or more animals of different species, with a view to determining their points of resemblance or dissimilarity.

If the organs, however, are subjected to a further analysis, they can be resolved into simple structures, apparently homogeneous, to which the name tissue has been given—*e.g.*, epithelial, connective, muscle, and nerve tissue. When the tissues are subjected to a microscopic analysis, it is found that they are not homogeneous in structure, but composed of still simpler elements, termed cells and fibers. The investigation of the internal structure of the organs, the physical properties and structure of the tissues, as well as the structure of their component elements, the cells and fibers, constitutes a department of anatomic science known as **histology,** or as it is prosecuted largely with the microscope, **microscopic anatomy.**

Human anatomy is that department of anatomic science which has for its object the investigation of the construction of the human body.

GENERAL STRUCTURE OF THE ANIMAL BODY

The body of every animal, from fish to man, may be divided into—

1. An axial portion, consisting of the head, neck, and trunk; and—
2. An appendicular portion, consisting of the anterior and posterior limbs or extremities.

The Axial Portion.—The axial portion of all mammals, to which class man zoölogically belongs, as well as of all birds, reptiles, amphibians, and osseous fish, is characterized by the presence of a bony, segmented axis, which extends in a longitudinal direction from before backward, and which is known as the vertebral column or backbone. In virtue of the existence of this column all the classes of animals just mentioned form one great division of the animal kingdom, *the Vertebrata*.

Each segment, or vertebra, of this axis consists of—

1. A solid portion, known as the body or centrum, and

2. A bony arch arising from the dorsal aspect and surmounted by a spine-like process.

At the anterior extremity of the body of the animal the vertebræ are variously modified and expanded, and, with the addition of new elements, form the skull; at the posterior extremity they rapidly diminish in size, and terminate in man in a short, tail-like process. In many animals, however, the vertebral column extends for a considerable distance beyond the trunk into the tail. The vertebral column may be regarded as the foundation element in the plan of organization of all the higher animals and the center around which the rest of the body is developed and arranged with a certain degree of conformity. In all vertebrate animals the bodies of the segments of the vertebral column form a partition which serves to divide the trunk of the body into two cavities—viz., the dorsal and the ventral.

The Dorsal Cavity.—The dorsal cavity is found not only in the trunk, but also in the head. Its walls are formed partly by the arches which arise from the posterior or dorsal surface of the vertebræ and partly by the bones of the skull. If a longitudinal section can be made through the center of the vertebral column, and including the head, the dorsal cavity will be observed running through its entire extent. Though for the most part it is quite narrow, at the anterior extremity it is enlarged and forms the cavity of the skull. This cavity is lined by a membranous canal, the neural canal, in which are contained the brain and the neural or spinal cord. Through openings in the sides of the dorsal cavity nerves pass out which connect the brain and spinal cord with all the structures of the body.

The Ventral Cavity.—The ventral cavity is confined mainly to the trunk of the body. Its walls are formed by muscles and skin, strengthened in most animals by bony arches, the ribs. Within the ventral cavity is contained a musculo-membranous tube or canal known as the alimentary or food canal, which begins at the mouth on the ventral side of the head, and, after passing through the neck and trunk, terminates at the posterior extremity of the trunk at the anus. It may be divided into mouth, pharynx, esophagus, stomach, small and large intestines.

In all mammals the ventral cavity is divided by a musculo-membranous partition into two smaller cavities, the thorax and abdomen. The former contains the lungs, heart and its great blood-vessels, and the anterior part of the alimentary canal, the gullet or esophagus; the latter contains the continuation of the alimentary canal—that is, the stomach and intestines—and the glands in connection with it, the liver and pancreas. In the posterior portion of the abdominal cavity are found the kidneys, ureters, and bladder, and in the female the organs of reproduction. The thoracic and abdominal cavities are each lined by a thin serous membrane, known, respectively, as the pleural and peritoneal membranes, which, in addition, are reflected over the surfaces of the organs contained within them.

The Surfaces of the Body.—The external surface of the body is covered by the skin. This is composed of an inner portion, the derma, and an outer portion, the epidermis. The former consists of connective-tissue fibers, blood-vessels, nerves, etc.; the latter of layers of scales or cells. Embedded within the skin are numbers of glands, which exude, in the different classes of animals, sweat, oily matter, etc. Projecting from the surface of the skin are hairs, bristles, feathers, claws. Beneath the skin are found muscles, bones, blood-vessels, nerves, etc.

The internal surface—the surface of the alimentary tract and associated cavities—is covered by mucous membrane.

The Appendicular Portion.—The appendicular portion of the body consists of two pairs of symmetric limbs, which project from the sides of the trunk, and which bear a determinate relation to the vertebral column. They consist fundamentally of bones, surrounded by muscles, blood-vessels, nerves and lymphatics. The limbs, though having a common plan of organization, are modified in form and adapted for prehension and locomotion in accordance with the needs of the animal.

Anatomic Systems.—All the organs of the body which have certain peculiarities of structure in common are classified by anatomists into systems—*e.g.*, the bones, collectively, constitute the bony or osseous system; the muscles, the nerves, the skin, constitute, respectively, the muscle, the nerve, and the tegumentary systems.

Physiologic Apparatus.—More important from a physiologic point of view than a classification of organs based on similarities of structure is the natural association of two or more organs acting together for the accomplishment of some definite object, and to which the term physiologic apparatus has been applied. While in the community of organs which together constitute the animal body each one performs some definite function, and the harmonious coöperation of all is necessary to the life of the individual, everywhere it is found that two or more organs, though performing totally distinct functions, are coöperating for the accomplishment of some larger or compound function in which their individual functions are blended—*e.g.*, the mouth, stomach, and intestines, with the glands connected with them, constitute the *digestive apparatus*, the object or function of which is the complete digestion of the food. The capillary blood-vessels and lymphatic vessels of the body, and especially those in relation to the villi of the small intestine, constitute the *absorptive apparatus*, the function of which is the introduction of new material into the blood. The heart and blood-vessels constitute the *circulatory apparatus*, the function of which is the distribution of blood to all portions of the body. The lungs and trachea, together with the diaphragm and the walls of the chest, constitute the *respiratory apparatus*, the function of which is the introduction of oxygen into the blood and the elimination from it of carbon dioxid and other injurious products. The kidneys, the ureters, and the bladder constitute the *urinary apparatus*. The skin, with its sweat-glands, constitutes the *perspiratory apparatus*, the functions of both being the excretion of waste products from the body. The liver, the pancreas, the mammary glands, as well as other glands, each form a *secretory apparatus* which elaborates some specific material necessary to the nutrition of the individual. The functions of these different physiologic apparatus—*e.g.*, digestion, absorption of food, elaboration of blood, circulation of blood, respiration, production of heat, secretion, and excretion—are classified as *nutritive functions*, and have for their final object the preservation of the individual and therefore the species.

The nerves and muscles constitute the *nervo-muscle apparatus*, the function of which is the production of motion. The eye, the ear, the nose, the tongue, and the skin, with their related structures, constitute, respectively, the *visual*, *auditory*, *olfactory*, *gustatory*, and *tactile apparatus*, the function of which, as a whole, is the reception of impressions and the transmission of nerve impulses to the brain, where they give rise to visual, auditory, olfactory, gustatory, and tactile sensations and volitional impulses.

The brain, in association with the sense organs, forms an apparatus related to mental processes. The larynx and its accessory organs—the lungs, trachea, respiratory muscles, the mouth and resonant cavities of the face—form the *vocal* and *articulating apparatus*, by means of which voice and articulate speech are produced. The functions exhibited by the apparatus just mentioned—viz., motion, sensation, language, mental and moral manifestations—are classified as *functions of relation*, as they serve to bring the individual into conscious relationship with the external world.

The ovaries and the testes are the essential reproductive organs, the former producing the germ-cell, the latter the sperm element. Together with their related structures—the fallopian tubes, uterus, and vagina in the female, and the urogenital canal in the male—they constitute the *reproductive apparatus* characteristic of the two sexes. Their coöperation results in the union of the germ-cell and sperm element and the consequent development of a new being. The function of reproduction serves to perpetuate the species to which the individual belongs.

The animal body is therefore not a homogeneous organism, but one composed of a large number of widely dissimilar but related organs. As all vertebrate animals have the same general plan of organization, there is a marked similarity both in form and structure among corresponding parts of different animals. Hence it is that in the study of human anatomy a knowledge of the form, construction, and arrangement of the organs in different types of animal life is essential to its correct interpretation; it follows also that in the investigation and comprehension of the complex problems of human physiology a knowledge of the functions of the organs as they manifest themselves in the different types of animal life is indispensable. As many of the functions of the human body are not only complex, but the organs exhibiting them are practically inaccessible to investigation, we must supplement our knowledge and judge of their functions by analogy, by attributing to them, within certain limits, the functions revealed by experimentation upon the corresponding organs of lower animals. This experimental knowledge, corrected by a study of the clinical phenomena of disease and the results of post-mortem investigations, forms the basis of modern human physiology.

CHAPTER II

CHEMIC COMPOSITION OF THE HUMAN BODY

Since it has been demonstrated that every exhibition of functional activity is associated with changes of structure, it has been apparent that a knowledge of the chemic composition of the body, not only when in a state of rest, but to a far greater degree when in a state of activity, is necessary to a correct understanding of the intimate nature of physiologic processes. Though the analysis of the dead body is comparatively easy, the determination of the successive changes in composition of the living body is attended with many difficulties. The living material, the bioplasm, is not only complex and unstable in composition, but extremely sensitive to all physical and chemic influences. The methods, therefore, which are employed for analysis destroy its composition and vitality, and the products which are obtained are peculiar to dead rather than to living material.

Chemic analysis, therefore, may be directed—

1. To the determination of the composition of the dead body.
2. To the determination of the successive changes in composition which the living bioplasm undergoes during functional activity.

A chemic analysis of the dead body, with a view to disclosing the substances of which it is composed, their properties, their intimate structure, their relationship to one another, constitutes what might be termed **chemic anatomy.** An investigation of the living material and of the successive changes it undergoes in the performance of its functions constitutes what has been termed **chemic physiology** or **physiologic chemistry.**

By chemic analysis the animal body can be reduced to a number of liquid and solid compounds which belong to both the inorganic and organic worlds. These compounds, resulting from a proximate analysis, have been termed proximate principles. That they may merit this term, however, they must be obtained in the form under which they exist in the living condition. The organic compounds consist of representatives of the carbohydrate, fat, and protein groups of organic bodies; the inorganic compounds consist of water, various acids, and inorganic salts.

The compounds or proximate principles thus obtained can be further resolved by an ultimate analysis into a small number of chemic elements which are identical with elements found in many other organic as well as inorganic compounds. The different chemic elements which are thus obtained, and the percentages in which they exist in the body, are as follows—viz., oxygen, 72 per cent.; hydrogen, 9.10; nitrogen, 2.5; carbon, 13.50; phosphorus, 1.15; calcium, 1.30; sulphur, 0.147; sodium, 0.10; potassium, 0.026; chlorin, 0.085; fluorin, iron, silicon, magnesium, iodine, in small and variable amounts.

THE CARBOHYDRATES

The carbohydrate compounds, which enter into the composition of the animal body, are mainly starches and sugar. In many respects they are closely related, and by appropriate means are readily converted into one another. In composition they consist of the elements carbon, hydrogen, and oxygen. As their name implies, the hydrogen and oxygen are present in these compounds in the proportion in which they exist in water, or as 2 : 1. The molecule of the carbohydrates above mentioned consists of either six atoms of carbon or a multiple of six; in the latter case the quantity of hydrogen and oxygen taken up by the carbon is increased, though the ratio remains unchanged.

The carbohydrates may be divided into three groups—viz., (1) *amyloses*, including starch, dextrin, glycogen, and cellulose; (2) *dextroses*, including dextrose, levulose, galactose; (3) *saccharoses*, including saccharose, lactose, and maltose. According to the number of carbon atoms entering into the second group (six), they are frequently termed monosaccharids; those of the third group, disaccharids—twice six; those of the first group, polysaccharids—multiples of six.

Though but few of the members of the carbohydrate group are constituents of the human body, many are constituents of the foods; on account of their importance in this respect, and their relation to one another, the chemic features of the more generally consumed carbohydrates will be stated in this connection.

Chemic Composition.—A chemic analysis of the carbohydrates shows that they consist of carbon hydrogen and oxygen though the percentage of these elements varies somewhat in different members of the group. The average percentage composition of several carbohydrates is as follows:

	C.	H.	O.
Starch	44.44	6.17	49.39
Dextrose	40.00	6.66	53.34
Saccharose	42.10	6.44	51.46

1. AMYLOSES, $(C_6H_{10}O_5)_n$.

Starch is widely distributed in the vegetable world, being abundant in the seeds of the cereals, leguminous plants, and in the tubers and roots of many vegetables. It occurs in the form of microscopic granules which vary in size, shape, and appearance, according to the plant from which they are obtained. Each granule presents a nucleus, or hilum, around which is arranged a series of eccentric rings, alternately light and dark. The granule consists of an envelope and stroma of cellulose, containing in its meshes the true starch material—*granulose*. Starch is insoluble in cold water and alcohol. When heated with water up to 70°C., the granules swell, rupture, and liberate the granulose, which forms an apparent solution; if present in sufficient quantity, it forms a gelatinous mass termed starch paste. On the addition of iodin, starch strikes a characteristic deep blue color; the compound formed—iodid of starch—is weak, the color disappearing on heating, but reappearing on cooling.

Boiling starch with dilute sulphuric acid (25 per cent.) converts it into dextrose. In the presence of vegetable diastase or animal ferments, starch is converted into maltose and dextrose, two forms of sugar.

Dextrin is a substance formed as an intermediate product in the transformation of starch into sugar (maltose). There are at least two principal varieties—*erythrodextrin*, which strikes a red color with iodin, and *achroödextrin*, which is without color when treated with this reagent. In the pure state dextrin is a yellow-white powder, soluble in water. In the presence of animal ferments erythrodextrin is converted into maltose.

Glycogen is a constituent of the animal liver, and, to a slight extent, of muscles, 0.5 to 0.9 per cent., and of tissues generally. In the tissues of the embryo it is especially abundant. When obtained in a pure state it is an amorphous, white powder. It is soluble in water, forming an opalescent solution. With iodin it strikes a port-wine color. In some respects it resembles starch, in others dextrin. Like vegetable starch, glycogen or animal starch can be converted by dilute acids and ferments into sugar (dextrose).

Cellulose is the basic material of the more or less solid framework of plants. It is soluble in ammoniacal solution of cupric oxid, from which it can be precipitated by acids. It is an amorphous powder. Cellulose is very stable toward dilute acids and alkalies. It is this property which is made use of in the technical preparation of cellulose, in order to free it from the other substances present in the plant material. When cellulose is treated with strong sulphuric acid, and after disintegration diluted with water and then boiled, it is completely hydrolyzed to dextrose.

2. DEXTROSES, $C_6H_{12}O_6$.

Dextrose, glucose, or **grape-sugar** is found in grapes, most sweet fruits, and honey, and as a normal constituent of liver, blood, muscles, and other animal tissues. In the disease diabetes mellitus it is found also in the urine.

When obtained from any source, it is soluble in water and in hot alcohol, from which it crystallizes in six-sided tables or prisms. As usually met with, it is in the form of irregular, warty masses. It is sweet to the taste. When examined with the polariscope, it will be found that dextrose turns the plane of polarized light to the right. It is therefore termed dextro-rotatory and has received its name from this fact.

It has for a long time been known that when sugar, cupric hydroxid, and an alkali—*e.g.*, sodium or potassium hydroxid—are present in solution, the sugar will abstract from the cupric hydroxid a portion of its oxygen, thus reducing it to a lower stage of oxidation giving rise to cuprous oxid. Sugar has a similar action on both silver and bismuth salts. On this property of sugar a standard solution of cupric hydroxid was suggested by Fehling which may be employed for both qualitative and quantitative tests for the presence of sugar in solution.

Fehling's Test Solution.—This is a solution of cupric hydroxid made alkaline by an excess of sodium or potassium hydroxid with the addition of sodium and potassium tartrate. It is made by dissolving cupric sulphate 34.64 grams, potassium hydroxid 125 grams, sodium and potassium tartrate 173 grams, in distilled water sufficient to make one liter.

The reaction is expressed by the following equation:

$$CuSO_4 + 2KOH = Cu(OH)_2 + K_2SO_4.$$

The object of the sodium and potassium tartrate is to dissolve the cupric hydroxid and hold it in solution.

For qualitative analysis it is only necessary to boil a cubic centimeter of this solution, diluted with 4 c.c. of water, in a test-tube; then add the suspected solution and again heat to the boiling-point. If sugar be present, the cupric hydroxid is reduced to the condition of a cuprous oxid, which shows itself as a red or orange-yellow precipitate. The color of the precipitate depends on the relative excess of either copper or sugar, being red with the former, orange or yellow with the latter. The delicacy of this test is shown by the fact that a few minims of this solution will detect in 1 c.c. of water the $\frac{1}{15}$ of a milligram of sugar. (Dextrose.)

For quantitative analysis, 10 c.c. of Fehling's solution, diluted with 40 c.c. of water, are heated in a porcelain capsule, to which the suspected solution is cautiously added from a buret until the blue color entirely disappears. The strength of this solution is such that 10 c.c. is decolorized by 50 milligrams of sugar (*dextrose*). Thus if 0.8 c.c. of the suspected solution, *e.g.*, urine, decolorizes 10 c.c. of Fehling's solution, then it contains 50 milligrams of sugar, from which the percentage of sugar in the urine can be determined.

The Fermentation Test.—All the sugars with the exception of lactose undergo reduction to simpler compounds, mainly alcohol and carbon dioxid, under the action of the yeast plant, *Saccharomyces cerevisiæ.* The change with dextrose is expressed in the following equation:

$$C_6H_{12}O_6 = 2C_2H_6O + 2CO_2.$$

Dextrose = Alcohol + Carbon Dioxid.

About 95 per cent. of the dextrose is so changed, the remaining 5 per cent. yielding secondary products—succinic acid, glycerin, etc. As a means of testing any solution for the presence of sugar this method may be adopted. It is generally very satisfactory. From the quantity of carbon dioxid and alcohol thus produced the quantity of sugar in the solution may be determined.

Levulose, or **fruit-sugar,** is found in association with dextrose as a constituent of many fruits. It is sweeter than dextrose and more soluble in both water and dilute alcohol. From alcoholic solutions it crystallizes in fine, silky needles, though it usually occurs in the form of a syrup.

Levulose is distinguished from dextrose by its property of turning the plane of polarized light to the left; the extent to which it does so, however, varies with the temperature and concentration of the solution. For this reason it is turned levulo-rotatory and has received its name from this fact.

Under the influence of the yeast plant it slowly undergoes fermentation, yielding the same products as dextrose. It also has a reducing action on cupric hydroxid.

Galactose is obtained by boiling milk-sugar (lactose) with dilute sulphuric acid. In many chemic relations it resembles dextrose. It is less soluble in water, however, crystallizes more easily, and has a greater dextrorotatory power. It also undergoes fermentation with the yeast plant.

3. SACCHAROSES, $C_{12}H_{22}O_{11}$.

Saccharose, or **cane-sugar,** is widely distributed throughout the vegetable world, but is especially abundant in sugar-cane, sorghum cane, sugar-beet, Indian corn, etc. It crystallizes in large monoclinic prisms. It is soluble in water and in dilute alcohol. Saccharose has no reducing power on cupric hydroxid, and hence its presence cannot be detected by Fehling's solution. It is dextro-rotatory. Boiled with dilute mineral, as well as with organic acids, saccharose combines with water and undergoes a change in virtue of which it rotates the plane of polarized light to the left, and hence the product was termed *invert* sugar. This latter has been shown to be a mixture of equal quantities of levulose and dextrose. This inversion of saccharose through hydration and decomposition is expressed in the following equation:

$$\begin{array}{c} C_{12}H_{22}O_{11} + H_2O = C_6H_{12}O_6 + C_6H_{12}O_6 \\ \text{Saccharose} + \text{Water} = \underbrace{\text{Levulose} + \text{Dextrose}}_{\text{Invert Sugar.}} \end{array}$$

Saccharose is not directly fermentable by yeast, but through the specific action of a ferment, *invertin* or *invertase*, secreted by the yeast plant, or the inverting ferment of the small intestine, it undergoes inversion, as previously stated, after which it is readily fermented, yielding alcohol and carbon dioxid.

Lactose is the form of sugar found exclusively in the milk of the mammalia, from which it can be obtained in the form of hard, white, rhombic prisms united with one molecule of water. It is soluble in water, insoluble in alcohol and ether. It is dextro-rotatory. It reduces cupric hydroxid, but to a less extent than dextrose. Dilute acids decompose it into equal quantities of dextrose and galactose. Lactose is not fermentable with yeast, but in the presence of the lactic acid bacillus it is decomposed into lactic acid, and finally into butyric acid, as expressed in the following equation:

$$\begin{array}{ccccc} C_{12}H_{22}O_{11} & + & H_2O & = & 4C_3H_6O_3 \\ \text{Lactose} & + & \text{Water} & = & \text{Lactic Acid.} \end{array}$$

$$\begin{array}{ccccccc} 2C_3H_6O_3 & = & C_4H_8O_2 & + & 2CO_2 & + & 2H_2 \\ \text{Lactic Acid} & = & \text{Buytric Acid} & + & \text{Carbon} & + & \text{Free} \\ & & & & \text{Dioxid} & & \text{Hydrogen.} \end{array}$$

Maltose is a transformation product of starch, and arises whenever the latter is acted on by malt extract or the diastatic ferments in saliva and pancreatic juice. The change is expressed by the following equation:

$$\begin{array}{ccccc} 2C_6H_{10}O_5 & + & H_2O & = & C_{12}H_{22}O_{11} \\ \text{Starch.} & & \text{Water.} & & \text{Maltose.} \end{array}$$

Maltose crystallizes in the form of white needles, which are soluble in water and in dilute alcohol. It is dextro-rotatory. In the presence of ferments and dilute acids maltose undergoes hydration and decomposition, giving rise to two molecules of dextrose. It has a reducing action on cupric hydroxid. Fermentation is readily caused by yeast, but whether directly or indirectly by inversion is somewhat uncertain.

Osazones.—All the sugars which possess the power of reducing cupric hydroxid are capable of combining with phenyl-hydrazin, with the formation of compounds termed osazones. The osazones so formed are crystalline in structure, but have different melting-points, varying degrees of solubility and optic properties, all of which serve to detect the various sugars and to distinguish one from the other. Of the different osazones, phenyl-glucosazone is the most characteristic, and occurs in the form of long, yellow needles. It may be obtained from dextrose by the following method: To 50 c.c. of a dextrose solution add 2 gm. of phenyl-hydrazin and 2 gm. of sodium acetate, and boil for an hour. On cooling, the osazone crystallizes in the form of long, yellow needles.

THE FATS

The fats constitute a group of organic bodies found in the tissues of both vegetables and animals. In the vegetable world they are largely found in fruits, seeds, and nuts, where they probably originate from a transformation of the carbohydrates. In the animal body the fats are found largely in the subcutaneous tissue, in the marrow of bones, in and around various internal organs and in milk. In these situations fat is contained in small, round or polygon-shaped vesicles, which are united by areolar tissue and surrounded by blood-vessels. At the temperature of the body the fat is liquid, but after death it soon solidifies from the loss of heat.

The fats are compounds consisting of carbon, hydrogen, and oxygen. The percentage composition of fat (stearin) is as follows: Carbon, 76.86; hydrogen, 12.36; oxygen, 10.78. The fat found in animals is a mixture, in varying proportions in different animals, of three neutral fats—*stearin*, *palmitin*, and *olein*. Each fat is a derivative of glycerin and the particular acid indicated by its name—*e.g.*, stearic acid, in the case of stearin, etc. The reaction which takes place in the combination of glycerin and the acid is expressed in the following equation:

$$\underset{\text{Glycerin.}}{C_3H_5(OH)_3} + \underset{\text{Stearic Acid.}}{3H.C_{18}H_{35}O_2} = \underset{\text{Stearin.}}{C_3H_5(C_{18}H_{35}O_2)_3} + \underset{\text{Water.}}{3H_2O.}$$

Hence, strictly speaking, the fats are compound ethers, in which the hydrogen of the organic acid is replaced by the trivalent radical, tritenyl, C_3H_5.

Stearin, $C_3H_5(C_{18}H_{35}O_2)_3$, is the chief constituent of the more solid fats. It is solid at ordinary temperatures, melting at 55°C., then solidifying again as the temperature rises, until at 71°C. it melts permanently. It crystallizes in square tables.

Palmitin, $C_3H_5(C_{16}H_{31}O_2)_3$ is a semifluid fat, solid at 45°C. and melting at 62°C. It crystallizes in fine needles, and is soluble in ether.

Olein, $C_3H_5(C_{18}H_{33}O_2)_3$, is a colorless, transparent fluid, liquid at ordinary temperatures, only solidifying at 0°C. It possesses marked solvent powers, and holds stearin and palmitin in solution at the temperature of the body.

Saponification.—When subjected to the action of superheated steam, a neutral fat is saponified—*i.e.*, decomposed into glycerin and the particular acid indicated by the name of the fat used: *e.g.*, stearic, palmitic, or oleic. The reaction is expressed as follows:

$$\underset{\text{Olein.}}{C_3H_5(C_{18}H_{33}O_2)_3} + \underset{\text{Water.}}{3H_2O} = \underset{\text{Glycerin.}}{C_3H_5(OH)_3} + \underset{\text{Oleic Acid.}}{3C_{18}H_{34}O_2}$$

The fat acids thus obtained are characterized by certain chemic features, as follows:

Stearic acid is a firm, white solid, fusible at 69°C. It is soluble in ether and alcohol, but not in water.

Palmitic acid occurs in the form of white, glistening scales or needles, melting at 62°C.

Oleic acid is a clear, colorless liquid, tasteless and odorless when pure. It crystallizes in white needles at 0°C.

If this saponification takes place in the presence of an alkali—*e.g.*, potassium hydroxid or sodium hydroxid—the acid produced combines at once with the alkali to form a salt known as a soap, while the glycerin remains in solution. The reaction is as follows:

$$\underset{\text{Potassium Hydroxid.}}{3KHO} + \underset{\text{Oleic Acid.}}{3C_{18}H_{34}O_2} = \underset{\text{Potassium Oleate.}}{3KC_{18}H_{33}O_2} + \underset{\text{Water.}}{3H_2O}$$

All soaps are, therefore, salts formed by the union of alkalies and fat acids. The sodium soaps are generally hard, while the potassium soaps are soft. Those made with stearin and palmitin are harder than those made with olein. If the soap is composed of lead, zinc, copper, etc., it is insoluble in water.

Emulsification.—When a neutral oil is vigorously shaken with water or other fluid, it is broken up into minute globules that are more or less permanently suspended; the permanency depending on the nature of the liquid. The most permanent emulsions are those made with soap solutions. The process of emulsification and the part played by soap can be readily observed by placing on a few cubic centimeters of a solution of sodium carbonate (0.25 per cent.) a small quantity of a perfectly neutral oil to which has been added 2 or 3 per cent. of a fat acid. The combination of the acid and the alkali at once forms a soap. The energy set free by this combination rapidly divides the oil into extremely minute globules. A spontaneous emulsion is thus formed.

THE PROTEINS

The proteins constitute a group of organic bodies which are found in both vegetable and animal tissues. Though present in all animal tissues, they are especially abundant in muscles and bones, where they constitute 20 per cent. and 30 per cent. respectively. Though genetically related, and possessing many features in common, the different members of the protein group are distinguished by characteristic physical and chemic properties which serve not only for their identification, but for their classification into more or less well-defined groups.

Chemic Composition.—A chemic analysis of proteins shows that they consist of carbon, hydrogen, oxygen, nitrogen and sulphur, though the percentage of each of these elements varies somewhat in the different proteins.

A certain number of proteins contain phosphorus while almost all of them contain different inorganic salts in varying amounts. The average percentage composition of several proteins is shown in the following analyses:

	C.	H.	N.	O.	S.	
Egg-albumin.........	52.9	7.2	15.6	23.9	0.4	(Würtz).
Serum-albumin.......	53.0	6.8	16.0	22.29	1.77	(Hammersten).
Casein...............	52.3	7.07	15.91	22.03	0.82	(Chittenden and Painter).
Myosin.........	52.82	7.11	16.77	21.90	1.27	(Chittenden and Cummins).

The molecular composition of the proteins is not definitely known and the formulæ which have been suggested are therefore only approximative. Leow assigns to albumin the formula $C_{72}H_{112}N_{18}O_{22}S$, while Schützenberger raises the numbers to $C_{240}H_{392}N_{65}O_{75}S_3$, either of which shows that the protein molecule is extremely complex.

Structure of the Protein Molecule.—From the large size of the protein molecule as indicated by its chemic composition it might be inferred that its structure was equally complex. This, modern investigation has shown to be the case.

When any one of the typical proteins, found in animal or vegetable tissues, is hydrolyzed by acids, alkalies and animal ferments under appropriate conditions, it can be resolved through a series of descending stages into relatively simple nitrogen-holding bodies termed *amino-acids* and *diamino-acids*, of which somewhat more than twenty have been isolated and their properties determined. The principal amino-acids are as follows: Glycocoll, alanin, leucin, isoleucin, amino-isovalerianic acid, serin, aspartic acid, glutamic acid, phenylalanin, tyrosin, prolin, tryptophan. The principal diamino-acids are as follows: Ornithin, lysin, histidin, arginin, cystin.

The protein molecule is therefore structurally complex. The manner in which these elementary compounds are arranged, united or grouped in any given protein, is practically unknown. More or less successful attempts have been made at the reconstruction of the protein molecule by synthetic methods, by the union of two or more of the amino-acids. A number of such compounds have been formed by the union of from two to ten or more amino-acids, all of them exhibiting many of the protein reactions. Such bodies are termed, according to their complexity, peptids and polypeptids.

Physical Properties.—As a class the proteins are characterized by the following properties:

1. **Indiffusibility.**—None of the proteins normally assume the crystalline form, and hence they are not capable of diffusing through parchment or an animal membrane. Peptone, a product of the digestion of proteins, is an exception as regards its diffusibility. As met with in the body, all proteins are amorphous, but vary in consistence from the liquid to the solid state. The colloid character of the proteins permits of their separation and purification from crystalloid diffusible compounds by the process of dialysis.
2. **Solubility.**—Some of the proteins are soluble in water, others in solutions of the neutral salts of varying degrees of concentration, in strong acids and alkalies. All are insoluble in alcohol and ether.
3. **Coagulability.**—Under the influence of heat and animal ferments, some of the proteins readily pass from the soluble liquid state to the insoluble solid state, attended by a permanent alteration in their chemic composition. To this change the term coagulation has been given. The various proteins, however, coagulate at different temperatures. Proteins are capable of precipitation without losing their solubility by ammonium sulphate, sodium chlorid, and magnesium sulphate.
4. **Fermentability.**—In the presence of specific microörganisms—bacteria—the proteins, owing to their complexity and instability, are prone

to undergo disintegration and reduction to simpler compounds. This decomposition or putrefaction occurs most readily when the conditions most favorable to the growth of bacteria are present—viz., a temperature varying from 25°C. to 40°C., moisture, and oxygen. The intermediate as well as the terminal products of the decomposition of the proteins are numerous, and vary with the composition of the protein and the specific physiologic action of the bacteria. Among the intermediate products is a series of alkaloid bodies, some of which possess marked toxic properties, known as ptomains. The toxic symptoms which frequently follow the ingestion of foods in various stages of putrefaction are to be attributed to these compounds. The terminal products are represented by hydrogen sulphid, ammonia, carbon dioxid, fats, phosphates, nitrates, etc.

Classification.—The animal proteins by virtue of their structural composition, their physical and chemic properties, permit of a provisional arrangement into three groups as follows: Simple proteins, conjugate proteins and protein derivatives.

SIMPLE PROTEINS

The simple proteins are so called because of the fact that when they are hydrolyzed they yield only α-amino- and diamino-acids. The members of this group are as follows:

PROTAMINS.

These proteins are derived for the most part from the heads of the spermatozoa of fish. They take their names from the species of fish from which they are obtained, *e.g.*, salmin (salmon), sturin (sturgeon), scombrin (mackerel), etc. Inasmuch as they respond to Piotrowski's test in a characteristic way they are regarded as true proteins. When subjected to hydrolysis they can be resolved into the diamino bodies, lysin, arginin and histidin, of which they constitute about 90 per cent., and a small number of the mono-amino-acids. Because of the fact that the diamino bodies, lysin, histidin and arginin contain 6 atoms of carbon they are known as the *hexone* bases. Inasmuch as the protamins contain practically but these three bodies, they are regarded as the simplest of all the proteins. Since a typical protein always yields on hydrolysis the hexone bases, in addition to a variable number of mono-amino-acids, it is believed that the usual protein is composed of a nucleus of the hexone bases to which is attached a variable number of mono-amino-acids. The proportions in which the bases exist in the nucleus and the proportions in which the amino-acids are united to the nucleus, vary in different proteins.

HISTONS.

The proteins embraced in this class comprise a series of compounds which are somewhat more complex than the protamins and less complex than the typical proteins; for on hydrolysis they not only yield the hexone bases but in addition a large number of mono-amino-acids. They are, therefore, intermediate in structural composition between the protamins and the usual proteins. Their protein character is indicated by their reaction to Millon's reagent and to Piotrowski's test. They are precipitated from neutral solution by alkaloid reagents. The histons are usually found in combination with nucleic acid, in the spermatozoa of most animals and especially in fish, and in the coloring matter (the hemoglobin) of the red corpuscles. The proteins of the tissues usually contain from 25 to 30 per cent. of histons.

ALBUMINS.

The members of this group are soluble in water, in dilute saline solutions, and in saturated solutions of sodium chlorid and magnesium sulphate. They are coagulated by heat, and when dried form an amber-colored mass.

(*a*) **Serum-albumin.**—This most important protein is found in blood, lymph, chyle, and some tissue fluids. It is obtained readily by precipitation from blood-serum, after the other proteins have been removed, on the addition of ammonium sulphate. When freed from saline constituents, it presents itself as a pale, amorphous substance, soluble in water and in strong nitric acid. It is coagulated at a temperature of 73°C., as well as by various acids—*e.g.*, citric, picric, nitric, etc. It has a rotatory power of −62.6°.

(*b*) **Egg-albumin.**—Though not a constituent of the human body, egg-albumin resembles the foregoing in many respects. When obtained in the solid form from the white of the egg, it is a yellow mass without taste or odor. Though similar to serum-albumin, it differs from it in being precipitated by ether, in coagulating at 54°C., and in having a lower rotatory power, −35.5°.

(*c*) **Lact-albumin.**—As its name implies, this protein is found in milk. It can be precipitated from milk-plasma by sodium sulphate after the precipitation of the other proteids by half saturation with ammonium sulphate. It slowly coagulates at 77°C.

(*d*) **Myo-albumin.**—This protein is found in muscle-plasma from which it subjects the plasma to fractional heat coagulation. At 73°C. myo-albumin coagulates.

GLOBULINS.

(*a*) **Serum-globulin or Paraglobulin.**—This protein, as its name implies, is found in blood-serum, though it is present in other animal fluids. When precipitated by magnesium sulphate or carbon dioxid, it presents itself as a flocculent substance, insoluble in water, soluble in dilute acids and alkalies, and coagulating at 75°C.

(*b*) **Fibrinogen.**—This protein is found in blood-plasma in association with serum-globulin and serum-albumin. It is also present in lymph-tissue fluids and in pathologic transudates. It can be obtained from blood-plasma which has been previously treated with magnesium sulphate on the addition of a saturated solution of sodium chlorid. It is soluble in dilute acids and alkalies, and coagulates at 56°C.

(*c*) **Paramyosinogen or Myosin.**—This protein is a constituent of the muscle-plasma from which it can be precipitated by a temperature of 47°C.

(*d*) **Myosinogen or Myogen.**—This protein is the chief constituent of the muscle-plasma and is of great nutritive value. During the living condition it is liquid, but after death it readily undergoes a chemic change and contributes to the formation of an insoluble protein known as myogen fibrin. It is soluble in dilute hydrochloric acid and dilute alkalies. It coagulates at 56°C.

(*e*) **Crystallin or Globulin.**—This is obtained by passing a stream of CO_2 through a watery extract of the crystalline lens.

SCLERO-PROTEINS (ALBUMINOIDS).

The sclero-proteins constitute a group of substances similar to the proteins in many respects, though differing from them in others. When obtained from the tissues, in which they form an organic basis, they are found to be amorphous, colloid, and when decomposed yield products similar to those of the true proteins. The principal members of this group are as follows:

(*a*) **Collagen, Ossein.**—These are two closely allied, if not identical, substances, found respectively in the white fibrous connective tissue and in bone. When the tendons of muscles, the ligaments, or decalcified bone are boiled for several hours, the collagen and ossein are converted into soluble gelatin, which, when the solution cools, becomes solid.

(*b*) **Chondrigen.**—This is supposed to be the organic basis of the more permanent cartilages. When the latter are boiled, they yield a substance which gelatinizes on cooling, and to which the name chondrin has been given. Chondrin, however, is not a pure gelatin, but has associated with it a compound protein known as chrondromucoid.

(*c*) **Elastin** is the name given to the substance composing the fibers of the yellow, elastic connective tissue.

(*d*) **Keratin** is the substance found in all horny and epidermic tissues, such as hairs, nails, scales, etc. It differs from most proteins in containing a high percentage of sulphur.

PHOSPHO-PROTEINS.

The two members of this group are distinguished by yielding on decomposition a protein which contains phosphorus. It was formerly regarded as a nuclein.

(*a*) **Caseinogen.**—This is the principal protein of milk, in which it exists in association with calcium in a form known as calcium-caseinogenate. It is *precipitated* by acetic acid and by magnesium sulphate. It is *coagulated* by rennin, though the nature of the process is not very clear. It was formerly taught that under the action of rennin, an enzyme of the gastric mucous membrane, caseinogen was separated into a solid portion, *casein* or *tyrein*, and a soluble portion. The cleavage action of rennin thus indicated has not been verified by subsequent investigations. It is more in accordance with the facts to assume that the process is a double one and that the action of rennin is to change the caseinogen to a soluble form, termed paracasein, after which the lime salts present react with the paracasein in such a manner as to cause it to assume the solid condition. Calcium phosphate seems to be the natural alkali necessary to this process, for if it be removed by dialysis, or precipitated by the addition of potassium oxalate, the casein will not be curdled by rennin, but it will nevertheless, undergo a change, for if the solution be treated as above and then boiled to destroy the rennin, it will curdle upon the addition of calcium salts.

(*b*) **Vitellin.**—Vitellin is a constituent of the vitellis or yolk of eggs. It differs from other proteins in the fact that it is semicrystalline in character. Though usually regarded as a nucleo-protein it is not definitely known whether or not it contains phosphorus in its composition.

CONJUGATED OR COMBINED PROTEINS

The conjugated proteins are compounds in which the protein molecule is combined with some other molecule or molecules, the chemic nature of which varies considerably in the different members of the group, *e.g.*, coloring matter, carbohydrates and nuclein. The chemic character of the non-protein substance furnishes the basis for the following classification:

CHROMO-PROTEINS.

(*a*) **Hemoglobin.**—Hemoglobin is the coloring matter of the red corpuscles, of which it constitutes about 30 per cent. of the total weight. It possesses the power of absorbing oxygen as it passes through the lung capillaries and of yielding it up to the tissues as it passes through the tissue capillaries. In the arterial blood it is known as oxyhemoglobin, and in the venous blood as deoxy- or reduced-hemoglobin. When hydrolyzed by acids or alkalies, hemoglobin undergoes a cleavage into a protein, globin, and a coloring matter, hemochromogen, containing iron, which is easily oxidized to hematin.

(*b*) **Myohematin.**—Myohematin is a protein supposed to be present in muscle. It has never been isolated, hence its chemic features are unknown. Spectroscopic examination indicates that it is capable of absorbing and again yielding up oxygen. For this reason it is believed to be a derivative of hemoglobin.

GLUCO-PROTEINS.

(*a*) **Mucin.**—Mucin is the protein which gives the mucus, secreted by the epithelial cells of the mucous membranes and related glands, its viscid, tenacious character. It is also a constituent of the intercellular substance of the connective tissues. It is readily precipitated by acetic acid. When heated with dilute acids, mucin undergoes a cleavage into a simpler protein and a carbohydrate termed mucose, which is capable of reducing Fehling's solution.

(*b*) **Mucoids.**—The mucoids resemble the mucins though differing from them in solubility and in not being precipitable from alkaline solutions by acetic acid. They are found in the vitreous humor, white of egg, cartilage, tendon, bone, and in other situations. Chondromucoid differs from other connective-tissue mucoids in the large amount of chondroitin-sulphuric acid obtained upon decomposition. When decomposed through the action of acid, the chondroitin-sulphuric acid yields sulphuric acid and a nitrogenous body—chondroitin, which in turn yields acetic acid and a new nitrogenous substance—chondrosin, which has a more strongly reducing action on Fehling's solution than dextrose. They differ slightly one from the other in properties and chemic composition. They yield on decomposition a carbohydrate.

NUCLEO-PROTEINS.

The nucleo-proteins are obtained from the nuclei and cell-substance of tissue-cells. Chemically they are characterized by the presence of phosphorus in relatively large amounts. When hydrolyzed, they separate into a protein and a nuclein. The nucleins derived from cell nuclei can be still further separated into a simpler protein and *nucleic* acid, which latter in turn yields phosphoric acid, carbohydrates—mostly pentoses, pyrimidine bases—thymine, cytosine, and uracyl, and the so-called purin bases, xanthin, hypoxanthin, adenin, and guanin. All nucleins which yield the purin bases are termed *true nucleins.*

DERIVATIVES OF PROTEIN

The protein derivatives include a variety of substances which arise through a process of hydrolysis of simple proteins under the action of enzymes and in the presence of acids and alkalies. The number of derivatives obtained between the first cleavage of the protein molecule and its final cleavage to amino-acids is large and will be presented at length in the paragraph relating to protein digestion. The chief derivatives are as follows:

INFRA-PROTEINS.

(*a*) **Acid-albumin.**—This is formed when a native albumin is digested with dilute hydrochloric acid (0.2 per cent.) or dilute sulphuric acid for some minutes. It is precipitated by neutralization with sodium hydroxid (0.1 per cent. solution). After the precipitate is washed, it is found to be insoluble in distilled water and in neutral saline solutions. In acid solutions it is not coagulated by heat.

(*b*) **Alkali-albumin.**—This is formed when a native albumin is treated with a dilute alkali—*e.g.*, 0.1 per cent. of sodium hydroxid—for five or ten minutes. On careful neutralization with dilute hydrochloric acid, it is precipitated. It is also insoluble in distilled water and in saline solutions; it is not coagulable by heat.

PROTEOSES, PEPTONES AND POLYPEPTIDS.

During the progress of the digestive process, as it takes place in the stomach and intestines, there is produced by the action of the gastric and pancreatic juices, out of the proteins of the food, a series of new proteins, known as proteoses, peptones and polypeptids. The chemic properties of these substances will be considered in connection with the process of digestion.

COAGULATED PROTEINS.

Although these proteins are not found as constituents of the animal organism, they possess much interest on account of their relation to prepared foods and to the digestive process. They are produced when solutions of egg-albumin, serum-albumin, or globulins are subjected to a temperature of 100°C. or to the prolonged action of alcohol. They are insoluble in water, in dilute acids, and in neutral saline solutions.

In this same group may be included also those coagulated proteins which are produced by the action of animal ferments on soluble proteins—*e.g.*, fibrin, myosin, casein.

(*a*) **Fibrin.**—Fibrin is derived from one of the blood proteins—viz., fibrinogen. It is not present under normal circumstances in the circulating blood, but makes its appearance after the blood is withdrawn from the vessels and at the time of coagulation. It can also be obtained by whipping the blood with a bundle of twigs, on which it accumulates. When freed from blood by washing under water, it is seen to consist of bundles of white elastic fibers or threads. It is insoluble in water, in alcohol, and ether. In dilute acids it swells, becomes transparent, and finally is converted into acid albumin. In dilute alkalies a similar change takes place, but the resulting product is an alkali-albumin. Fibrin possesses the property of decomposing hydrogen dioxid, H_2O_2—*i.e.*, liberating oxygen, which accumulates in the form of bubbles on the fibrin. On incineration fibrin yields an ash which contains calcium phosphate and magnesium phosphate.

Two views are held as to the origin of fibrin: first that it is the result of the action of a special enzyme, termed *thrombin* on fibrinogen, though the nature of the action is not very clear; second that it is the result of a definite combination, physio-chemic in character, of fibrinogen with thrombin which, however, is not regarded as an enzyme, inasmuch as it is not destroyed by boiling, but a definite compound partaking of the nature of an organic colloid. The amount of fibrin formed from fibrinogen will be proportional to the amount of thrombin present.

(*b*) **Myosin fibrin** and **myogen fibrin** are two insoluble proteins developed out of the two chief proteins of muscle-plasma. Their development after death is believed to be the cause of the stiffening of the muscles. It is not definitely known whether this is the result of the action of a special enzyme or not.

(*c*) **Casein.**—Casein is derived from the chief protein of milk—caseinogen—by the action of a special ferment known as rennin or chymosin. This ferment is a constituent of gastric juice.

The Color Reactions of Proteins.—When proteins are present in solution, they may be detected by the following color reactions—viz.,

1. Xanthoproteic. The solution is boiled with nitric acid for several minutes, when the protein assumes a light yellow color. After the solution has cooled, the addition of ammonia changes the color to an orange or amber-red, due to the presence of phenylalanin and tyrosin.
2. The rose-red reaction. The solution is boiled with acid nitrate of mercury (Millon's reagent) for a few minutes, when the coagulated protein turns a purple-red color. This color is attributed to the presence of tyrosin.
3. The blue-violet reaction. To the solution is added an excess of sodium hydroxide, at least an equal volume, and then drop by drop, a very dilute solution of copper sulphate. A blue-violet color is produced, which deepens somewhat on heating, but no further change ensues.

This is also known as Piotrowski's test: As this same color is developed with the substance biuret, it is also known as the *biuret reaction.* Biuret is formed by heating urea to 180°C and driving off ammonia.

Precipitation Tests.—Proteins in solution may be *precipitated* by nitric acid, acetic acid and potassium ferrocyanid, picric acid, copper sulphate, tannin, alcohol, etc. As stated in a foregoing paragraph, certain of the proteins, *e.g.*, fibrinogen, caseinogen and myosinogen, will undergo, by the action of an animal ferment a change of state by virtue of which they become solid. To this process the term *ferment coagulation* is applied. The solidification of proteins by the action of heat is designated *heat coagulation.*

INORGANIC CONSTITUENTS

The inorganic compounds and mineral constituents obtained from the solids and fluids of the body are very numerous, and, in some instances, quite abundant. Though many of the compounds thus obtained are undoubtedly derivatives of the tissues and necessary to their physical and physiologic activity, others, in all probability, are decomposition products, or transitory constituents introduced with the food. Of the inorganic compounds, the following are the most important:

WATER.

Water is the most important of the inorganic constituents, as it is indispensable to life. It is present in all the tissues and fluids without exception, varying from 99 per cent. in the saliva to 80 per cent. in the blood, 75 per cent. in the muscles to 2 per cent. in the enamel of the teeth. The total quantity contained in a body weighing 75 kilograms (165 pounds) is 52.5 kilograms (115 pounds). Much of the water exists in a free condition, and forms the chief part of the fluids, giving to them their characteristic degree of fluidity. Possessing the capability of holding in solution a large number of inorganic as well as some organic compounds, and being at the same time diffusible, it renders an interchange of materials between all portions of the body possible. It aids in the absorption of new material into the blood and tissues, and at the same time it transfers waste products from the tissues to the blood, from which they are finally eliminated, along with the water in which they are dissolved. A portion of the water is chemically combined with other tissue constituents and gives to the tissues their characteristic physical properties. The consistency, elasticity, and pliability are, to a large extent, conditioned by the amount of water they contain. The total quantity of water eliminated by the kidneys, lungs, and skin amounts to about 3 kilograms (6½ pounds) daily.

CALCIUM COMPOUNDS.

Calcium phosphate, $Ca_3(PO_4)_2$, has a very extensive distribution throughout the body. It exists largely in the bones, teeth, and to a slight extent in cartilage, blood, and other tissues. Milk contains 0.27 per cent. The solidity of the bones and teeth is almost entirely due to the presence of this salt, and is, therefore, to be regarded as necessary to their structure. It enters into chemic union with the organic matter, as shown by the fact that it cannot be separated from it except by chemic means, such as immersion in hydrochloric acid. Though insoluble in water, it is held in solution in the blood and milk by the protein constituents, and in the urine by the acid phosphate of soda. The total quantity of calcium phosphate which enters into the formation of the body has been estimated at 2.5 kilograms. The amount eliminated daily from the body has been estimated at 0.4 gm., a fact which indicates that nutritive changes do not take place with much rapidity in those tissues in which it is contained.

Calcium carbonate, $CaCO_3$, is present in practically the same situations in the body as the phosphate, and plays essentially the same rôle. It is, however, found in the crystalline form, aggregated in small masses in the internal ear, forming the otoliths, or ear stones. Though insoluble, it is held in solution by the carbonic acid diffused through the fluids.

Calcium fluorid, CaF_2, is found in bones and teeth.

SODIUM COMPOUNDS.

Sodium chlorid, $NaCl$, is present in all the tissues and fluids of the body, but especially in the blood, 0.6 per cent., lymph, 0.5, and pancreatic juice, 0.25 per cent. The entire quantity in the body has been estimated at about 200 gm. Sodium chlorid is of much importance in the body as it determines and regulates to a large extent the phenomena of diffusion which are there constantly taking place. The ingested water is absorbed into the blood largely in consequence of the percentage of this salt which it contains. The normal percentage of sodium chlorid in the blood-plasma assists in maintaining the shape and structure of the red blood-corpuscles by determining the amount of water entering into their composition. The same is true of other tissue elements.

Sodium chlorid also influences favorably the general nutritive process, though the manner in which it acts is not very clear. During its existence in the body it undergoes chemic transformations or decompositions, yielding its chlorin to form the potassium chlorid of the blood-corpuscles and muscles and to form the hydrochloric acid of the gastric juice.

Sodium phosphate, Na_2HPO_4, is found in all solids and fluids of the body, to which, with but few exceptions, it imparts an alkaline reaction. This is especially true of blood, lymph, and tissue fluids generally. It is essential to physiologic action that all tissue elements should be bathed by an alkaline medium.

Sodium carbonate, Na_2CO_3, is generally found in association with the preceding salt. As it is an alkaline compound, it also assists in giving to the blood and lymph their characteristic alkalinity. In carnivorous animals the sodium phosphate is the more abundant, while in the herbivorous animals the sodium carbonate is the more abundant.

Sodium sulphate, Na_2SO_4, is present in many of the tissues and fluids, especially in the urine. Though introduced in the food, it is also, in all probability, formed in the body from the decomposition and oxidation of the proteids.

POTASSIUM COMPOUNDS.

Potassium chlorid, KCl, is met with in association with sodium chlorid in almost all situations in the body. It preponderates, however, in the tissue elements, especially in the muscle tissue, nerve tissue, and red corpuscles. The plasma with which these structures are bathed contains but a very small amount of this salt, but, as previously stated, a relatively large amount of sodium chlorid. Though introduced to some extent in the food, it is very likely that it is also formed through the decomposition of the sodium chlorid.

Potassium phosphate, K_2HPO_4, is found in association with sodium phosphate in all the fluids and solids. As it has similar chemic properties, its functions are practically the same.

Potassium carbonate, K_2CO_3, is generally found with the preceding salt.

MAGNESIUM COMPOUNDS.

Magnesium phosphate, $Mg_3(PO_4)_2$, is found in all tissues, in association with calcium phosphate, though in much smaller quantity.

Magnesium carbonate, $MgCO_3$, occurs only in traces in the blood.

IRON COMPOUNDS.

Iron is a constituent of the coloring-matter of the blood. Traces, however, are also found in lymph, bile, gastric juice, and in the pigment of the eyes, skin and hair. The amount of iron contained in a body weighing 70 kilograms is about 2.2 gm. It exists under various forms—*e.g.*, ferric oxid, and in combination with organic compounds.

Iodin is found in a number of organs—thyroid gland, lungs, ovaries, liver, hypophysis, small intestines as well as in the blood and bile. The iodine content of the thyroid gland is eight to ten times that of all the other organs. The active ingredient of the thyroid colloid is the iodin-containing substance called thyroidin. It is contained in that portion of the protein which is soluble in physiological salt solution and precipitated upon half saturation with ammonium sulphate. This portion is apparently a globulin —called thyreoglobulin, and contains an easily separated carbohydrate group. The thyroid glands of new-born children are iodin free.

Chemic analysis thus shows that the chemic elements into which the compounds may be resolved by an ultimate analysis do not exist in the body in a free state, but only in combination, and in characteristic proportions, to form compounds whose properties are the resultant of those of the elements. Of the four principal elements which make up 97 per cent. of the body, O, H, N are extremely mobile, elastic, and possessed of great atomic heat. C, H, N are distinguished for the narrow range of their affinities, and for their chemic inertia. C possesses the greatest atomic cohesion. O is noted for the number and intensity of its combinations.

As the properties of the compounds formed by the union of elements must be the resultants of the properties of the elements themselves, it follows that the ternary compounds, starches, sugars, and fats must possess more or less inertia, and at the same time instability; while in the more complex proteids, in which sulphur and phosphorus are frequently combined with the four principal elements, molecular instability attains its maximum. As all the foregoing compounds possess in varying degrees the properties of inertia and instability, it follows that living matter must possess corresponding properties, and the capability of undergoing unceasingly a series of chemic changes, both of composition and decomposition, in response to the chemic and physical influences by which it is surrounded, and which underlie all the phenomena of life.

PRINCIPLES OF DISSIMILATION

In addition to the previously mentioned compounds—viz., carbohydrates, fats, proteids, and inorganic salts—there is obtained by chemic analysis from the tissues and fluids of the body:

1. A number of organic acids, such as acetic, lactic, oxalic, butyric, propionic, etc., in combination with alkaline and earthy bases.
2. Organic compounds, such as alcohol, glycerin, cholesterin.
3. Pigments, such as those found in bile and urine.
4. Crystallizable nitrogen-holding bodies, such as urea, uric acid, xanthin, hippuric acid, creatin, creatinin, etc.

While some few of these compounds may possibly be regarded as necessary to the physiologic integrity of the tissues and fluids, the majority of them are to be regarded as products of dissimilation of the tissues and foods in consequence of functional activity, and represent stages in their reduction to simpler forms previous to being eliminated from the body.

CHAPTER III

PHYSIOLOGY OF THE CELL

A histologic analysis of the organs and tissues of the animal body shows that they can be resolved into ultimate elements, termed cells, which may, therefore, be regarded as the primary units of structure. Though cells vary considerably in shape, size, and chemic composition in the different tissues of the adult body, they are, nevertheless, descendants from typical cells, known as embryonic or undifferentiated cells, the first offspring of the fertilized ovum. Ascending the line of embryonic development, it will be found that every organized body originates in a single cell—the ovum. As the cell is the elementary unit of all tissues, the function of each tissue must be referred to the function of the cell. Hence the cell may be defined as the primary anatomic and physiologic unit of the organic world, to which every exhibition of life, whether normal or abnormal, is to be referred.

Structure of Cells.—Though cells vary in shape and size and internal structure in different portions of the body, a typical cell may be said to consist mainly of a gelatinous substance forming the body of the cell, termed *cytoplasm* or *bioplasm*, in which is embedded a smaller spheric body, the *nucleus*. Within the nucleus there is frequently seen a still smaller body, the *nucleolus*. The shape of the adult cell varies according to the tissue in which it is found; when young and free to move in a fluid medium, the cell assumes a spheric form, but when subjected to pressure, may become cylindric, fusiform, polygonal, or stellate. Cells vary in size within wide limit, ranging from 7.7μ ($\frac{1}{3200}$ of an inch, the diameter of a red blood-corpuscle), to 135μ ($\frac{1}{200}$ of an inch, the diameter of the large cells in the gray matter of the spinal cord). (See Fig. 1.)

The **cytoplasm** consists of a soft, semifluid, gelatinous material, varying somewhat in appearance in different tissues. Though frequently homogeneous, it often exhibits a finely granular appearance under medium powers of the microscope. Young cells consist almost entirely of clear cytoplasm. Mature cells contain, according to the tissue in which they are found, material of an entirely different character—*e.g.*, small globules of fat, granules of glycogen, mucigen, pigments, digestive ferments, etc. Under high powers of the microscope the cytoplasm is found to be pervaded by a network of fibers, termed *spongioplasm*, in the meshes of which is contained a clearer and more fluent substance, the *hyaloplasm*. The relative amount of these two constituents varies in different cells, the proportion of hyaloplasm being usually greater in young cells. The arrangement of the fibers forming the spongioplasm also varies, the fibers having sometimes a radial direction, in others a concentric disposition, but most frequently being distributed evenly in all directions. In many cells the outer portion of the cell protoplasm undergoes chemic changes and is transformed into a thin, transparent, homogeneous membrane—the *cell membrane*—which completely incloses the cell substance. The cell membrane is permeable to water and watery solutions of various inorganic and organic substances. It is, however, not an essential part of the cell.

The **nucleus** is a small vesicular body embedded in the cytoplasm near the center of the cell. In the resting condition of the cell it consists of a distinct membrane, composed of *amphipyrenin*, inclosing the nuclear contents. The latter consists of a homogeneous amorphous substance—the nuclear matrix—in which is embedded the nuclear network. It can often be seen that a portion of one side of the nucleus, called the pole, is free from this network. The main cords of the network are arranged as **V**-shaped loops about it. These main cords send out secondary branches or twigs, which, uniting with one another, complete the network. The nuclear cords are composed of granules of *chromatin*—so called because of its affinity for certain staining materials—held together by an achromatin substance known as *linin*. Besides the nuclear network, there are embedded in the nuclear matrix one or more small bodies composed of *pyrenin*, known as *nucleoli*. At the pole of the nucleus, either within or just without in the cytoplasm, is a small body, the *centrosome*, or pole corpuscle.

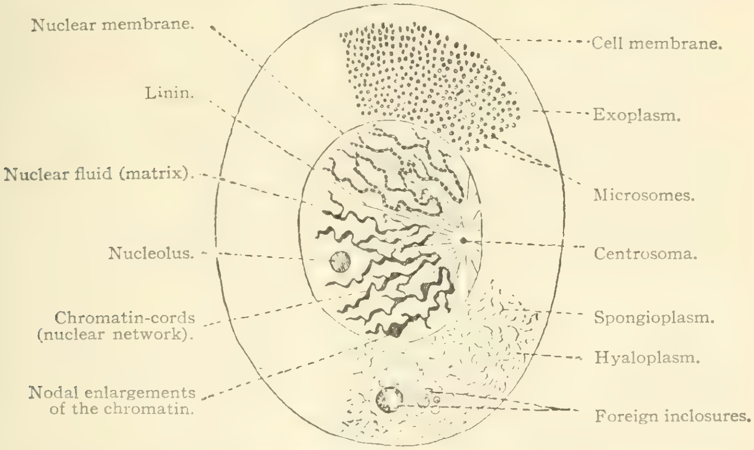

FIG. 1.—DIAGRAM OF A CELL. Microsomes and spongioplasm are only partly drawn.—(*Stohr.*

Chemic Composition of the Cell.—The composition of living bioplasm is difficult of determination, for the reason that all chemic and physical methods employed for its analysis destroy its vitality, and the products obtained are peculiar to dead rather than to living matter. Moreover, as bioplasm is the seat of extensive chemic changes, it is not easy to determine whether the products of analysis are crude food constituents or cleavage or disintegration products. Nevertheless, chemic investigations have shown that even in the living condition bioplasm is a highly complex compound—the resultant of the intimate union of many different substances. About 75 per cent. of bioplasm consists of water and 25 per cent. of solids, of which the more important compounds are various nucleo-proteins (characterized by their large percentage of phosphorus), globulins, lipoids, such as lecithin (a phosphorized fat) and cholesterin (a monatomic alcohol) and possibly fat and carbohydrates. Inorganic salts, especially the potassium, sodium, and calcium chlorids and phosphates, are almost invariable and essential constituents.

MANIFESTATIONS OF CELL LIFE

Growth, the Maintenance of Nutrition, and Reproduction.—All cells exhibit three fundamental properties of life—viz., growth, the maintenance of their nutrition, and reproduction. Growth is an increase in size. When newly reproduced all cells are extremely small, but in consequence of their organization and the character of their surrounding medium, they gradually grow until they attain the size characteristic of the adult state.

Nutrition may be defined as the sum of the processes concerned in the maintenance of the physiologic condition of the cell and includes both growth and repair. So long as this is accomplished, the cells and the tissues which are formed by them continue to exhibit their functions or their characteristic modes of activity. Both growth and nutrition are dependent on the power which living material possesses of not only absorbing nutritive material from the surrounding medium, the lymph, but of subsequently assimilating it, organizing it, transforming it into material like itself and endowing it with its own physiologic properties.

In the physiologic condition the living material of the cell, the bioplasm, is the seat of a series of chemic changes which vary in degree from moment to moment in accordance with the degree of functional activity, and on the continuance of which all life phenomena depend. Some of these chemic changes are related to or connected with the molecules of the living material, while others are connected with the food material supplied to them. Of the chemic changes occurring within the molecules some are destructive, dissimilative or disintegrative in character, whereby the molecule is in part eventually reduced through a series of descending chemic stages to simpler compounds which, apparently of no use in the cell, are eliminated from it. It is, therefore, said that the living material undergoes molecular disintegration as a result of functional activity. To these changes the term *katabolism* is also applied. Other of these changes are constructive, assimilative or integrative in character, whereby a part at least of the food material furnished by the blood-plasma is transformed through a series of ascending chemic stages into living material, and whereby it is repaired and its former physiologic condition restored. It is, therefore, said that the living material undergoes molecular integration as a preparation for functional activity. To these changes the term *anabolism* is also applied. During the course of its physiologic activities the cell bioplasm produces materials of an entirely different character which vary with the cell, such as fat, glycogen, mucigen, pigments, ferments, etc., which are generally spoken of as metabolic products.

Living material has also a temperature varying in degree in different species of animals as well as in different parts of the same animal. Here as elsewhere the temperature is due to heat liberated from organic compounds through disruption and subsequent oxidation to simpler compounds. Though some of the heat liberated may come from the tissue molecules, the larger part by far comes from the food molecules—sugar, fat, and protein, constituents of the fluids circulating in the tissue spaces. These foods carry into the body potential energy, ultimately derived from the sun. When they are disrupted and oxidized the potential energy is transformed into kinetic energy which manifests itself for the most part as heat. To the sum total of all the chemic changes occurring in tissues and foods the term *metabolism* is given.

There is, however, much difference of opinion as to the extent to which the living material is metabolized and to the actual disposition of the food materials, and especially the proteins, or their cleavage products, the amino-acids. Thus Voit contended that the tissue molecules are comparatively stable in composition and under ordinary conditions of nutrition do not undergo any material change during either rest or activity, and that metabolism is confined to the food materials occupying spaces in and around the living cell. The cause which initiates this metabolism is unknown, but is supposed to reside in the cell, if it is not a property of the cell itself. Because of the fact that but a very small amount of sugar or fat enters into the composition of bioplasm it is generally admitted that these foods are metabolized in the tissue spaces and in the manner just alluded to. The problem, however, is different in the case of the proteins. Voit contended, as previously stated, that the proteins of the tissue molecules, which he distinguished as tissue proteins, do not metabolize to any appreciable extent and confined practically all protein metabolism to the food proteins, now distinguished as amino-acids, circulating in the tissue spaces and which he characterized as circulating proteins. Even in starvation the tissue proteins, as such, do not metabolize until they have been disintegrated in consequence of chemic changes and transformed into circulating proteins.

Pflüger, however, asserted that the circulating proteins cannot be metabolized as such but that they must first be built up into tissue proteins. The metabolism of protein is, therefore, confined, in this view, to the molecules of the living material. It is possible, however, that both views are correct and that in the physiologic condition the activity of the tissues is attended by a partial destruction of the protein molecules which is followed in turn by construction out of amino-acids during the subsequent rest, but that the greater part of the protein metabolism takes place outside the cell, though in contact with it.

Though the cell is, therefore, the seat of two opposing processes, assimilation and dissimilation, it retains under normal conditions an average physiologic state, and so long as this is the case it is in a condition of *nutritive equilibrium* and capable of performing its various functions.

Though the foregoing statements are applied to the individual cell they are equally applicable to the body as a whole, inasmuch as the organs and tissues of which it consists are composed of cells. The body grows in size and maintains its nutrition, by the introduction of food materials which are utilized in part, for the repair of the tissues which have undergone molecular disintegration in consequence of activity, and in part for the liberation of energy. As a result of the disintegration or the metabolism of tissue and food materials, products such as carbon dioxid, urea, etc., are formed which, apparently of no further use, are discharged from the body by eliminating organs as the kidney, lungs, skin, etc. Assimilation and dissimilation are constantly taking place. If the food assimilated and metabolized exactly replaces the tissues dissimilated and the food metabolized the body will retain a condition of nutritive equilibrium.

To the metabolism that takes place in the tissue protein the term *endogenous* protein metabolism is given while to that which takes place in the tissue fluids the term *exogenous* protein metabolism is given.

Reproduction.—Cells reproduce themselves in the higher animals in two ways—by direct division and by indirect division, or karyokinesis. In the former the nucleus becomes constricted, and divides without any special grouping of the nuclear elements. It is probable that this occurs only in disintegrating cells, and never in a physiologic multiplication. In division by karyokinesis (Fig. 2) there is a progressive rearranging and definite grouping of the nucleus, the result of which changes is the division of the centrosome, the chromatin, and the rest of the nucleus into two equal portions, which form the nuclei. Following the division of the nuclei, the protoplasm divides. The process may be divided into three phases:

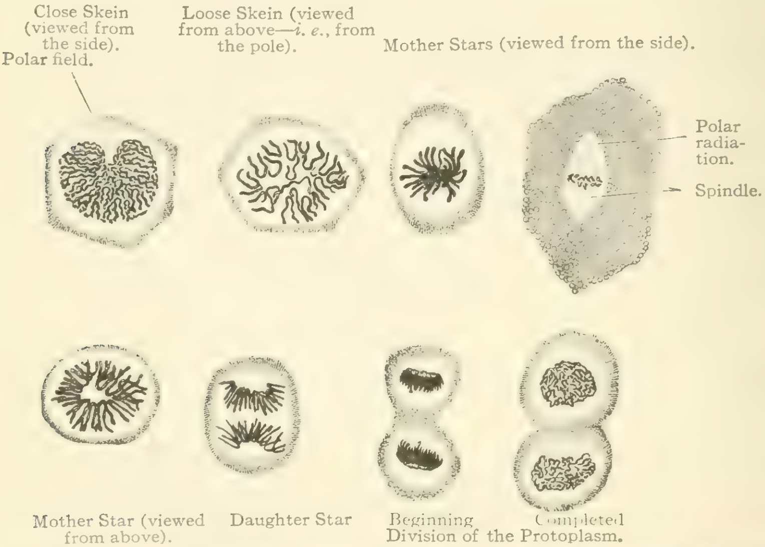
Close Skein (viewed from the side).
Polar field.
Loose Skein (viewed from above—*i. e.*, from the pole).
Mother Stars (viewed from the side).
Polar radiation.
Spindle.
Mother Star (viewed from above).
Daughter Star
Beginning
Completed
Division of the Protoplasm.

FIG. 2.—KARYOKINETIC FIGURES OBSERVED IN THE EPITHELIUM OF THE ORAL CAVITY OF A SALAMANDER. The picture in the upper right-hand corner is from a section through a dividing egg of Siredon pisciformis. Neither the centrosomes nor the first stages of the development of the spindle can be seen by this magnification. ×560.—(*Stöhr.*)

1. Prophase.—The centrosome, at first small and lying within the nucleus, increases in size and moves into the protoplasm, where it lies near the nucleus, surrounded by a clear zone, from which delicate threads radiate through an area known as the *attraction sphere*. The nucleus enlarges and becomes richer in chromatin. The lateral twigs of the chromatin cords are drawn in, while the main cords become much contorted. These cords have a general direction transverse to the long axis of the cell, and parallel to the plane of future cleavage. They are seen as **V**-shaped segments or loops, *chromosomes*, having their closed ends directed toward a common center, the *polar field*, while the other ends interdigitate on the opposite side of the nucleus—the antipole. The polar field corresponds to the area occupied by the centrosome. This arrangement is known as the *close skein;* but as the process goes on, the chromosomes become thicker, shorter and less contorted, producing a

much looser arrangement, known as the *loose skein.* During the formation of the loose skein, the centrosome divides into two portions, which move apart to positions at the opposite ends of the long axis of the nucleus. At the same time delicate achromatin fibers make their appearance, arranged in the form of a double cone, the apices of which correspond in position to the centrosomes. This is known as the *nuclear spindle.* During the prophase the nuclear membrane and the nucleoli disappear.

2. The Metaphase.—The two centrosomes are at opposite ends of the long axis of the nucleus, each surrounded by an attraction sphere, now called the *polar radiation.* The chromosomes become yet shorter and thicker, and move toward the equator of the nucleus, where they lie with their closed ends toward the axis, presenting the appearance, when seen from the poles, of a star—the so-called mother star, or monaster. While moving toward the equator of the nucleus, and often earlier, each chromosome undergoes longitudinal cleavage, the sister loops remaining together for a time. Upon the completion of the monaster, one loop of each pair passes to each pole of the nucleus, guided, and perhaps drawn by the threads of the nuclear spindle. The separation of the sister segments begins at their apices, and as the open ends are drawn apart they remain connected by delicate achromatin filaments drawn out from the chromosomes. This separation of the daughter chromosomes, and their movement toward the daughter centrosomes, is called *metakinesis.* As they approach their destination, we have the appearance of two stars in the nucleus—the *daughter stars,* or diasters.
3. Anaphase.—The daughter stars undergo, in reverse order, much the same changes that the mother star passed through. The chromosomes become much convoluted, and perhaps united to one another, the lateral twigs appear, and the chromatin resumes the appearance of the resting nucleus. The nuclear spindle, with most of the polar radiation, disappears, and the nucleoli and the nuclear membrane reappear, thus forming two complete daughter nuclei. Meanwhile the protoplasm becomes constricted midway between the young nuclei. This constriction gradually deepens until the original cell is divided, with the formation of two complete cells.

Physiologic Properties of Bioplasm.—All living bioplasm possesses properties which serve to distinguish and characterize it—viz., irritability, conductivity, and motility.

Irritability, or the power of reacting in a definite manner to some form of external excitation, whether mechanic, chemic, or electric, is a fundamental property of all living bioplasm. The character and extent of the reaction will vary, and will depend both on the nature of the bioplasm and the character and strength of the stimulus. If the bioplasm be muscle, the response will be a contraction; if it be gland, the response will be a secretion; if it be nerve, the response will be a sensation or some other form of nerve activity.

Conductivity, or the power of transmitting molecular disturbances arising at one point to all portions of the irritable material, is also a characteristic feature of all bioplasm. This power, however, is best developed in that form of bioplasm found in nerves, which serves to transmit, with extreme rapidity, molecular disturbances arising at the periphery to the brain, as well as from the brain to the periphery. Muscle bioplasm also possesses the same power in a high degree.

Motility, or the power of executing apparently spontaneous movements, is exhibited by many forms of cell bioplasm. In addition to the molecular movements which take place in certain cells, other forms of movement are exhibited, more or less constantly, by many cells in the animal body—*e.g.*, the waving of cilia, the ameboid movements and migrations of white blood-corpuscles, the activities of spermatozoa, the projection of pseudopodia, etc. These movements, arising without any recognizable cause, are frequently spoken of as spontaneous. Strictly speaking, however, all protoplasmic movement is the resultant of natural causes, the true nature of which is beyond the reach of present methods of investigation.

CHAPTER IV

HISTOLOGY OF THE EPITHELIAL AND CONNECTIVE TISSUES

1. EPITHELIAL TISSUE

The **epithelial tissue** consists of one or more layers of cells resting on a homogeneous membrane, the other side of which is abundantly supplied with blood-vessels and nerves. The form of the epithelial cell varies in different situations, and may be flattened, cuboid, spheroid or columnar. (See Figs. 4, 5, and 6.) The form of the cell in all instances is related to some specific function. When arranged in layers or strata, the cells are cemented together by an intercellular substance.

The epithelial tissue forms a continuous covering for the surfaces of the body. The external investment (the skin) and the internal investment (the mucous membrane, which lines the entire alimentary canal as well as associated body cavities) are both formed, in all situations, by the homogeneous basement membrane, covered with one or more layers of cells. The glands of the skin, the lungs and the glands in connection with the alimentary canal and the uro-genital apparatus are formed of the same elemental structures. All materials, therefore, whether nutritive, secretory, or excretory, must pass through epithelial cells before they can enter into the formation of the blood or be eliminated from it. The nutrition of the epithelial tissue is maintained by the nutritive material derived from the blood diffusing itself into and through the basement membrane. Chemically, the epithelial cells of the epidermis—hair, nails, etc.—are composed of a sclero-protein (keratin), a small quantity of water, and inorganic salts. In other situations, especially on the mucous membranes, the cells consist largely of mucin, in association with other proteins. The consistency of epithelium varies in accordance with external influences, such as the presence or absence of moisture, pressure, friction, etc. This is well seen in the skin of the palms of the hands and the soles of the feet—situations where it acquires its greatest density. In the alimentary canal, in the lungs, and in other cavities, where the reverse conditions prevail, the epithelium is extremely soft. Epithelial tissues also possess

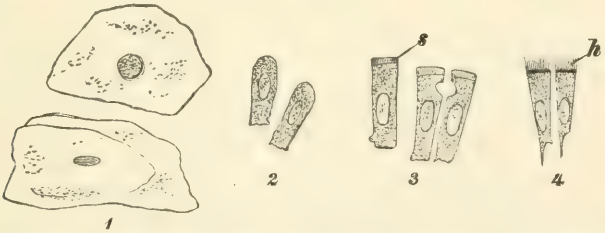

FIG. 3.—EPITHELIAL CELLS OF RABBIT, ISOLATED. × 560. 1. Squamous cells (mucous membrane of mouth). 2. Columnar cells (corneal epithelium). 3. Columnar cells, with cuticular border, *s* (intestinal epithelium). 4. Ciliated cells; *h*, cilia (bronchial epithelium).—(*Stöhr.*)

varying degrees of cohesion and elasticity—physical properties which enable them to resist considerable pressure and distention without having their physiologic integrity destroyed. Inasmuch as these tissues are poor conductors of heat, they assist in preventing too rapid radiation of heat from the body, and coöperate with other mechanisms in maintaining the normal temperature. The physiologic activity of all epithelial tissue depends on a due supply of nutritive material derived from the blood, which not only maintains its nutrition, but affords those materials out of which are formed the secretions of the glands, whether of the skin or mucous membrane.

The cells lining the blood-vessels, the lymph-vessels, the peritoneal, pleural, pericardial, and other closed cavities are usually termed *endothelial* cells. The cells in these situations are flat, irregular in shape, with borders more or less wavy or sinuous in outline.

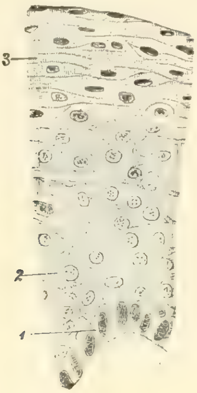

Fig. 4.—Stratified Squamous Epithelium (Larynx of Man). × 240. 1. Columnar cells. 2. Prickle-cells. 3. Squamous cells.—(*Stöhr.*)

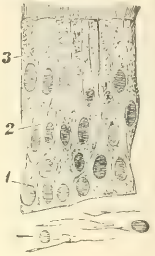

Fig. 5.—Stratified Ciliated Epithelium. × 560. From the respiratory nasal mucous membrane of man. 1. Oval cells. 2. Spindle-shaped cells. 3. Columnar cells.—(*Stohr.*)

Functions of Epithelial Tissue.—In succeeding chapters the form, chemic composition, and functions of epithelial cells will be considered in connection with the functions of the organs of which they constitute a part. In this connection it may be stated in a general way that the functions of the epithelial tissues are:

1. To serve on the surface of the body as a protective covering to the underlying structures which collectively form the true skin, thus protecting them from the injurious influences of moisture, air, dust, microörganisms, etc., which would otherwise impair their vitality. Wherever continuous pressure is applied to the skin, as on the palms of the hands and soles of the feet, the epithelium increases in thickness and density, and thus prevents undue pressure on the nerves of the true skin. The density of the epidermis enables it to resist, within limits, the injurious influence of acids, alkalies, and poisons.
2. To promote absorption. Inasmuch as the skin and mucous membranes cover the surfaces of the body, it is obvious that all nutritive material entering the body must first traverse the epithelial tissue. Owing to their density, however, the epithelial cells covering the skin play but a feeble rôle as absorbing agents in man and the higher animals. The

epithelium of the mucous membrane of the alimentary canal, particularly that of the small intestine, is especially adapted, from its situation, consistency, and properties, to play the chief rôle in the absorption of new materials from the canal. The epithelium lining the air-vesicles of the lungs is engaged in promoting the absorption of oxygen and the exhalation of carbon dioxid.

3. To form secretions and excretions. Each secretory gland connected with the surfaces of the body is lined by epithelial cells, which are actively concerned in the formation of the secretion peculiar to the gland. Each excretory organ is similarly provided with epithelial cells, which are engaged either in the production of the constituents of the excretion or in their removal from the blood.

2. THE CONNECTIVE TISSUES

The **connective tissues**, in their collective capacity, constitute a framework which pervades the body in all directions, and, as the name implies, serve as a bond of connection between the individual parts, at the same time affording a basis of support for the muscle, nerve, and gland tissues. The connective-tissue group includes a number of varieties, among which may be mentioned the areolar, adipose, retiform, white fibrous, yellow elastic, cartilaginous and osseous. Notwithstanding their apparent diversity, they possess many points of similarity. They have a common origin, developing from the same embryonic material; they have much the same structure, passing imperceptibly into one another, and perform practically the same functions.

Areolar Tissue.—This variety is found widely distributed throughout the body. It serves to unite the skin and mucous membrane to the structures on which they rest; to form sheaths for the support of blood-vessels, nerves, and lymphatics; to unite into compact masses the muscular tissue of the body, etc. Examined with the naked eye, it presents the appearance of being composed of bundles of fine fibers interlacing in every direction. In the embryonic state the elements of this form of connective tissue are united by a ground substance, gelatinous in character. In the adult state this substance shrinks and largely disappears, leaving intercommunicating spaces of varying size and shape, from which the tissue takes its name. When subjected to the action of various reagents, and examined microscopically, the bundles can be shown to consist of extremely delicate, colorless, transparent, wavy fibers, which are cemented together by a ground substance composed largely of mucin. Other fibers are also observed, which are distinguished by a straight course, a sharp, well-defined outline, a tendency to branch and unite with adjoining fibers, and to curl up at their extremities when torn. From their color and elasticity they are known as yellow elastic fibers. Distributed throughout the meshes of the areolar tissue are found flattened, irregularly branched, or stellate corpuscles, connective-tissue corpuscles, plasma cells, and granule cells.

Adipose Tissue.—This tissue, which exists very generally throughout the body, though found most abundantly beneath the skin, around the kidneys, and in the bones, is practically but a modification of areolar tissue. In these situations it presents itself in small masses or lobules of varying size and shape, surrounded and penetrated by the fibers of connective tissue. (See Fig. 6.) Microscopic examination shows that these masses consist of small vesicles or cells, round, elliptical or polyhedral in shape, depending somewhat on pressure. (See Fig. 7.) Each vesicle consists of a thin, colorless, protoplasmic membrane, thickened at one point, in which a nucleus can usually be detected. This membrane incloses a globule of fat, which during life is in the liquid state. It is composed of olein, stearin, and palmitin. The origin of the fat is to be referred to a synthesis of a fat-acid and glycerin on the part of the cell material or of an enzyme contained therein. As fat granules accumulate, at the expense of the cell protoplasm, they gradually coalesce, until there remains but a thin stratum of the protoplasm, which forms the wall of the vesicle. Adipose tissue may, therefore, be regarded as areolar tissue, in which, and at the expense of some of its elements, fat is stored for the future needs of the organism. A diminution of food, especially of fat and carbohydrates, is promptly followed by an absorption of fat by the blood-vessels and by its transference to the tissues, where it is either utilized for tissue construction or for oxidation purposes. In the situations in which adipose tissue is found it serves, by its chemic and physical properties, to assist in the prevention of a too rapid radiation of heat from the body, to give form and roundness, and to diminish angularities, etc.

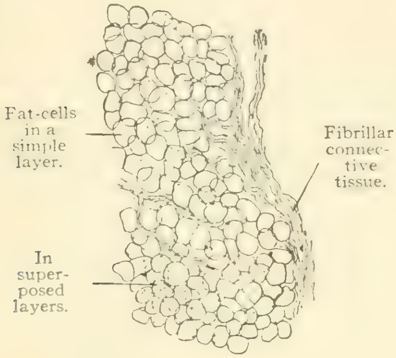

FIG. 6.—ADIPOSE TISSUE.—(*Stöhr*.)

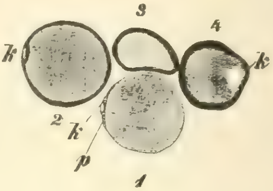

FIG. 7.—FAT-CELLS FROM THE AXILLA OF MAN. 1. The equator of the cell in focus. 2. The objective somewhat elevated. 3, 4. Forms changed by pressure. *p*. Traces of protoplasm in the vicinity of the flat nucleus *k*.—(*Stöhr*.)

Retiform and **adenoid tissue** are also modifications of areolar tissue. The meshes of the former contain but little ground substance, its place being taken by fluids; the meshes of the latter contain large numbers of lymph corpuscles.

Fibrous Tissue.—This variety of connective tissue is widely distributed throughout the body. It constitutes almost entirely the ligaments around the joints, the tendons of the muscles, the membranes covering organs such as the heart, liver, nerve system, bones, etc. All fibrous tissue, wherever found, can be resolved into elementary bundles, which on microscopic examination are seen to consist of delicate, wavy, transparent, homogeneous fibers, which pursue an independent course, neither branching nor uniting with adjoining fibers. (See Fig. 8.) A small amount of ground substance serves to hold them together. Fibrous tissue is tough and inextensible, and in consequence is admirably adapted to fulfil various mechanical functions in the body. It is, however, quite pliant, bending easily in all directions. When boiled, fibrous tissue yields gelatin, a derivative of collagen.

Elastic Tissue.—The fibers of elastic tissue are usually associated in varying proportions with the white fibrous tissue; but in some structures—as the ligamentum nuchæ, the ligamenta subflava, the middle coat of the larger blood-vessels—the elastic fibers are almost the only elements present, and give to these structures a distinctly yellow appearance. The fibers throughout their course give off many branches, which unite with adjoining branches to form a more or less close network. As the name implies, these fibers are highly elastic, and are capable of being extended as much as 60 per cent. of their length before breaking. (See Fig. 9.)

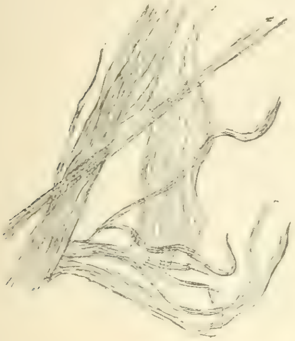

Fig. 8.—Connective-tissue Bundles of Various Thicknesses of the Intermuscular Connective Tissue of Man. × 240.—(*Stöhr.*)

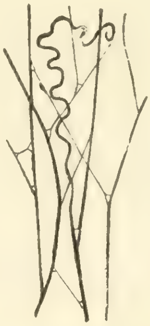

Fig. 9.—Elastic Fibers of the Subcutaneous Areolar Tissue of a Rabbit.—(After *Schäfer.*)

Cartilaginous Tissue.—This form of connective tissue differs from the preceding varieties chiefly in its density. As a rule, it is firm in consistency, though somewhat elastic. It is opaque, bluish-white in color, though in thin sections translucent. All cartilaginous tissues consist of connective-tissue cells embedded in a solid ground substance. According to the amount and texture of the ground substance, three principal varieties may be distinguished:

1. *Hyaline cartilage*, in which the cells, relatively few in number, are embedded in an abundant quantity of ground substance (Fig. 10, A.) The body of the cells is in many instances distinctly marked off from the surrounding substance by concentric lines of fibers, which form a capsule for the cell. Repeated division of the cell substance takes place, until the whole capsule is completely occupied by daughter cells. The ground substance is pervaded by minute channels, which communicate on one hand with the spaces around the cells, and on the other with lymph-spaces in the connective tissue surrounding the cartilage. By means of these channels, nutritive fluid can permeate the entire structure. Hyaline cartilage is found on the ends of the long bones, where it enters into the formation of the joints; between the ribs and sternum, forming the costal cartilage, as well as in the nose and larynx.

2. *White fibro-cartilage*, the ground substance of which is pervaded by white fibers, arranged in bundles or layers, between which are scattered the usual encapsulated cells. (See Fig. 10,C.) White fibro-cartilage is tough, resistant, but flexible, and is found in joints where strength and fixedness are required. Hence it is present between the vertebræ, forming the intervertebral discs, between the condyle of the lower jaw and the glenoid fossa, in the knee-joint, around the margins of the joint cavities, etc. In these situations it assists in maintaining the apposition of the bones, in giving a certain degree of mobility to the joints, and in diminishing the effects of shock and pressure imparted to the bones.

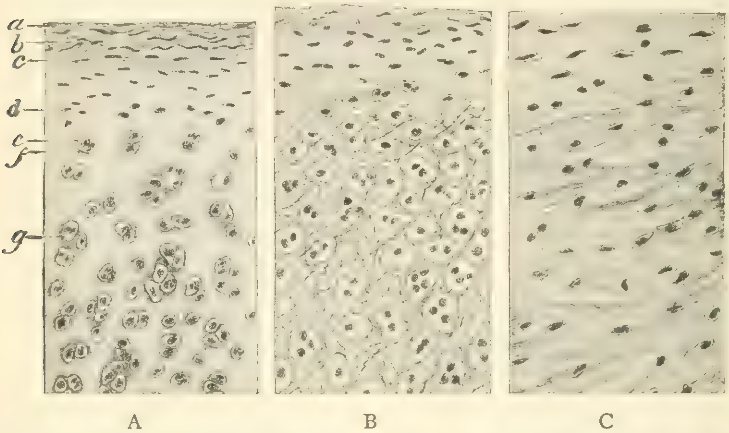

FIG. 10.—THE THREE TYPES OF CARTILAGE: A, HYALINE; B, ELASTIC; C, FIBROUS.—(*Radasch*). a, b, Outer and inner layers of perichondrium; c, young cartilage cells; d, older cartilage cells; e, f, capsule; g, lacuna.

3. *Yellow fibro-cartilage*, the ground substance of which is pervaded by opaque, yellow elastic fibers, which form, by the interlacing of their branches, a complicated network, in the meshes of which are to be found the usual corpuscles. (See Fig. 10,B.) As these fibers are elastic, they impart to the cartilage a very considerable degree of elasticity. Yellow fibro-cartilage is well adapted, therefore, for entering into the formation of the external ear, epiglottis, Eustachian tube, etc.—structures which require for their functional activity a certain degree of flexibility and elasticity.

Osseous Tissue.—Osseous tissue, as distinguished from bone, is a member of the connective-tissue group, the ground substance of which is permeated with insoluble lime salts, of which the phosphate and carbonate are the most abundant. Immersed in dilute solutions of hydrochloric acid, they can be converted into soluble salts and dissolved out. The osseous matrix left behind is soft and pliable. When boiled, it yields gelatin.

A thin, transverse section of a decalcified bone, when examined microscopically, reveals a number of small, round, or oval openings, which represent transverse sections of canals which run through the bone, for the most part in a longitudinal direction, though frequently anastomosing with one another. These so-called Haversian canals in the living state contain blood-vessels and lymphatics. (See Fig. 11.)

Around each Haversian canal is a series of concentric laminæ, composed of white fibers. Between every two laminæ are found small cavities (lacunæ), from which radiate in all directions small canals (canaliculi), which communicate freely with one another. The Haversian canals, with their associated lacunæ and canaliculi, form a system of intercommunicating passages, which circulate lymph destined for the nourishment of bone. Each lacuna contains the bone corpuscle, which bears a close resemblance to the usual branched connective-tissue corpuscle, and whose function appears to be the maintenance of the nutrition of the bone.

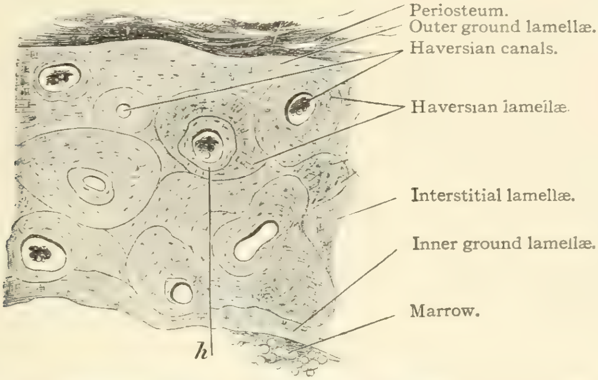

FIG. 11.—FROM A CROSS-SECTION OF A METACARP OF MAN. × 50. The Haversian canals contain a little marrow (fat-cells). Resorption line at *h*.—(*Stöhr*).

The surface of every bone in the living state is invested with a fibrous membrane, the periosteum, except where it is covered with cartilage. The inner surface of this membrane is loose in texture, and supports a fine plexus of capillary blood-vessels and numerous protoplasmic cells—the osteoblasts. As this layer is directly concerned in the formation of bone, it is spoken of as the *osteogenetic* layer.

A section of a bone shows that it is composed of two kinds of tissue—compact and cancellated. The compact is dense, resembling ivory, and is found on the outer portion of the bone; the cancellated is spongy, and appears to be made up of thin, bony plates, which intersect one another in all directions, and is found in greatest abundance in the interior of the bones. The shaft of a long bone is hollow. This central cavity, which extends from one end of the bone to the other, as well as the interstices of the cancellated tissue, is filled in the living state with marrow. The marrow or medulla is composed of a connective-tissue framework supporting blood-vessels. In its meshes are to be found characteristic bone cells or osteoblasts, the function of which is supposed to be the formation of bone. In the long bones the marrow is yellow, from the presence in the connective-tissue corpuscle of fat globules. In the cancellated tissue, near the extremities of the long bones, this fatty deposition does not take place to the same extent, and the marrow appears red. The cells of the red marrow are believed to give birth indirectly to the red blood-corpuscles.

Physical and Physiologic Properties of Connective Tissues.—Among the physical properties may be mentioned consistency, cohesion, and elasticity. Their *consistency* varies from the semiliquid to the solid state, and depends mainly on the quantity of water which enters into their composition. Their *cohesion*, except in the softer varieties, is very considerable, and offers great resistance to traction, pressure, torsion, etc. In all the movements of the body, in the contraction of muscles, in the performance of work, the consistence and cohesion of these tissues play most important rôles. Wherever the various forms of connective tissue are found, their chemic composition and structure are in relation to their functions. If traction be the preponderating force, the structure becomes fibrous as in ligaments and tendons, and the cohesion greatest in the longitudinal direction. If pressure be exerted in all directions, as upon membranes, the fibers interlace and offer a uniform resistance. When pressure is exerted in a definite direction, as on the extremities of the long bones, the tissue becomes expanded and cancellated. The lamellæ of the cancellated tissue arrange themselves in curves which correspond to the direction of the greatest pressure or traction. Extensibility is not a characteristic feature, except in those forms containing an abundance of yellow elastic fibers. The elasticity is an essential factor in many physiologic actions. It not only opposes and limits forces of traction, pressure, torsion, etc., but on their cessation returns the tissues or organs to their original condition. Elasticity thus assists in maintaining the natural form and position of the organs by counterbalancing and opposing temporarily acting forces.

The Skeleton.—The connective tissues in their entirety constitute a framework which presents itself under two aspects: (1) As a solid, bony skeleton, situated in the trunk and limbs, affording attachment for muscles and viscera; (2) as a fine, fibrous skeleton, found everywhere throughout the body, connecting the various viscera and affording support for the epithelial, muscle, and nerve tissues.

CHAPTER V

THE PHYSIOLOGY OF MOVEMENT

Of the four phenomena presented by an animal, that which more immediately interests the physiologist is movement, for the reason that it is not only the animal's most characteristic form of activity, and that which serves to distinguish it in the main from forms of vegetable life, but its solution affords an explanation of many physiologic processes occurring within the human body. It is also for this reason that movement constitutes for the most part the subject-matter of physiologic experimentation.

The movements of the body may for convenience be divided into two groups, viz., external and internal.

The External or Skeleto-muscle Movements.—The external movements are exhibited mainly by the head and extremities and may be either special as when the animal changes the relation of one part of the body to another, or general, as when it changes its position relatively to the environment as in the various acts of locomotion. The external movements are the result of the coöperation of the bones of the skeleton and the muscles which are attached to them. The skeleton imparts, nevertheless, a certain degree of rigidity and fixity to the body; were it not for this the body would be but a shapeless mass and incapable of performing any of its characteristic external movements.

The joints of the skeleton permit various parts of the body to move and to change their relation to each other. Without the presence of joints such as are found in the vertebral column and in the limbs, external movements would be impossible. The muscles impart movements to various parts of the body. This they do by suddenly shortening and widening whereby their extremities are approximated. The majority of the muscles of the body are attached to the bones in such a manner that when their form is altered, they change not only the relation of the bones with reference to each other, but perhaps also the individual's relation to surrounding objects. The muscles thus become the active organs in both motion and locomotion, in contradistinction to the bones which may be regarded as the passive organs in the performance of the corresponding movements.

In the execution of the movements the animal, of necessity, meets with various forms of resistance, viz., gravity, cohesion, friction, etc., which tend to oppose the movement. When its different parts are applied or directed, either volitionally and in a determinate manner, or non-volitionally and in an indeterminate or reflex manner, to the overcoming of these opposing forces in the environment, the animal may be said to be doing work.

In the animal as in the physical machine, work is accomplished by the intermediation of levers. In the animal machine, the levers are found in the bones of the skeleton and more particularly in the long bones of the extremities, the fulcra of which, the points around which they move, lie in the joints.

That a lever may be effective as an instrument for the accomplishment of work it must not only be capable of moving around its fulcrum, but it must at the same time be acted on by two opposing forces, one passive, the other active. In the movements of the bony levers of the animal body, the passive forces to be overcome are largely those connected with the environment, *e.g.*, gravity, cohesion, friction, etc., the active forces by which these are opposed and overcome through the mediation of the bony levers, are found in the muscles attached to them. The muscles are therefore to be regarded as the seat of those active energies that impart movement to the levers.

The Internal or Vasculo- and Viscero-muscle Movements and Gland Activities.—The internal movements are exhibited by the viscera, the vascular apparatus and by glands, and, though less obvious, are no less characteristic.

The viscera undergo variations in size from moment to moment as a result of the contraction and relaxation of the non-striated muscle fibers, composing in part their walls and thus regulate the reception and discharge of their contents.

The vascular apparatus, and its adjunct, the lymph-vessel apparatus, is engaged in the distribution of blood and nutritive material throughout the body. The cavities of the heart are alternately increased and diminished in size by the alternate relaxation and contraction of the muscle-fibers composing the walls of the heart. During the relaxation the cavities fill with blood and during the contraction the blood is driven through the vessels in opposition to the friction presented by their walls; while the vessels themselves and especially the arteries, by virtue of the presence of elastic fibers and the non-striated muscle-fibers in their walls, increase and decrease in caliber from moment to moment and thus regulate the amount of blood flowing through them in accordance with the physiologic needs of the organ to which they are distributed.

The glands and more especially their epithelial investments are the seat of certain molecular movements the result of which is the production and discharge of a secretion destined to play a more or less important part in the maintenance of the activities of the body.

In the performance of their functions these organs also meet resistances, *e.g.*, cohesion, friction, elasticity, etc., and when they are applied to the overcoming of these resistances or forces, as they are in the performance of their functions, it can also be said that they too are doing work. The coöperation of external and internal organs is necessary, however, not only for the maintenance of the life of the animal but also for the accomplishment of external work.

Tissue Stimuli.—The various tissues of the body, mentioned in foregoing paragraphs, though irritable do not possess spontaneity of action, but require for the manifestation of their characteristic forms of activity the application of a stimulus.

Thus the skeletal muscles and glands though capable of being excited to activity by various artificial stimuli, require for the exhibition of their normal activity the arrival of the physiologic stimulus, the *nerve impulse*, developed in and transmitted to them by the nerve-tissue.

The visceral and vascular muscles though apparently capable of being

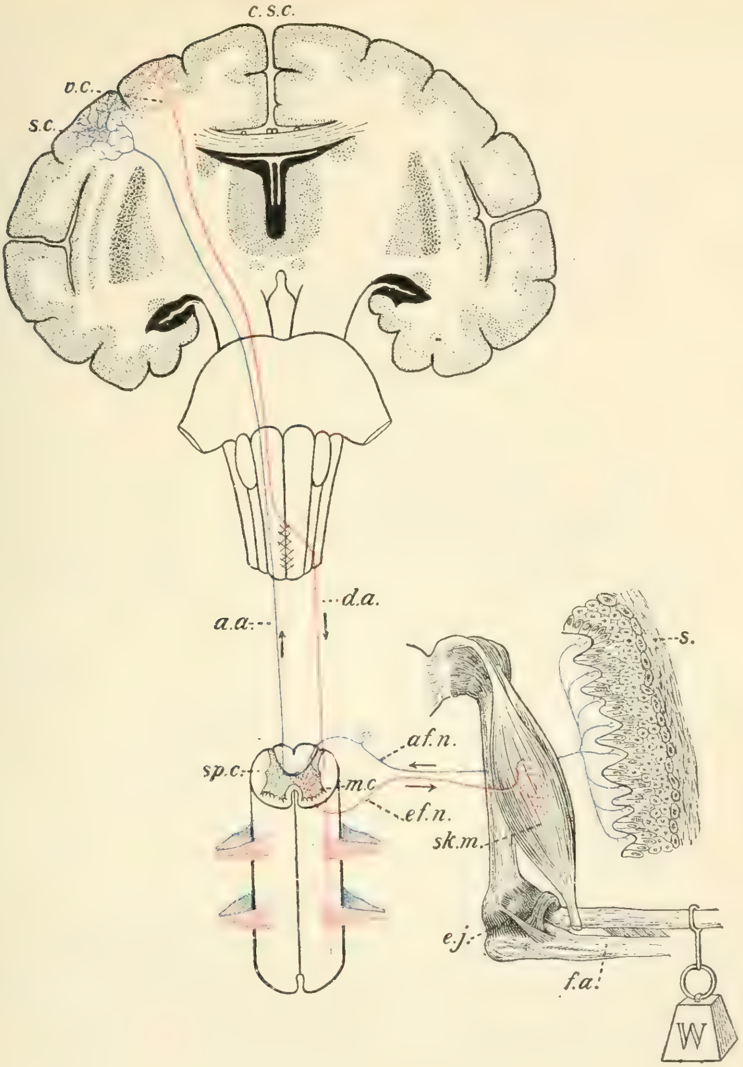

Fig. 12.—Diagram Showing the Relaton of Skeletal, Muscle and Nerve Tissues. (*G. Bachman.*) *f.a.* Bones of the forearm representing the skeletal tissue; ***e.j.*** the elbow-joint, the fulcrum of the lever formed by the bones of the forearm; *W.* a weight acting in a downward direction and representing the passive force of gravity; ***sk.m.*** a skeletal muscle acting in an upward direction and the source of the active power to be applied to the lever; ***sp.c.*** transection of the spinal cord showing the relation of the white and the gray matter: ***m.c.*** a motor cell in the anterior horn of the gray matter; ***ef.n.*** an efferent nerve-fiber connecting the motor cell from which it arises with the skeletal muscle and contained in the ventral roots of the spinal nerves; *af.n.* an afferent nerve-fiber arising from the ganglion cell along its course and connecting the skin, *s.*, on the one hand with the spinal cord on the other hand and contained in the dorsal roots of the spinal nerves; ***c.s.c.*** coronal section of the cerebrum showing the relation of the gray to the white matter; ***v.c.*** a volitional or motor cell; *d.a.* a descending axon or nerve-fiber connecting the volitional cell from which it arises with the motor cell in the spinal cord; *s.c.* a sensor cell; *a.a.* an ascending axon or nerve-fiber connecting a receptive cell from which it arises (not shown in the diagram) with the sensor cell in the gray matter of the cerebrum. The nerve-fibers which pass outward from the spinal cord to the glands, blood-vessels, and the muscle walls of the viscera, have for the sake of simplicity been omitted from the diagram.

excited to activity by agencies other than the nerve impulse are nevertheless augmented or inhibited in their activity from moment to moment by nerve impulses.

It is evident therefore that the activities of the organs and tissues which are engaged in promoting the work of the body are excited to action and controlled by the nerve-tissue, a fact which presupposes an anatomic connection between them.

For an understanding of the mode of excitation of the motor organs and the manner in which they coöperate in the performance of any given movement, a brief preliminary account of the general arrangement and mode of action of the nerve-tissue will be found helpful.

The General Relation of the Nerve-tissue to Peripheral Organs.—The nerve-tissue is arranged partly in masses contained within the cavities of the head and spinal column (the encephalon or brain and spinal cord), forming the central organs of the nerve system, and partly in the form of cords or nerves (the cranial and spinal nerves), forming the peripheral organs of the nerve system. The latter connect the former not only with muscles, glands, blood-vessels, and viscera, but with the skin, mucous membranes, etc., as well.

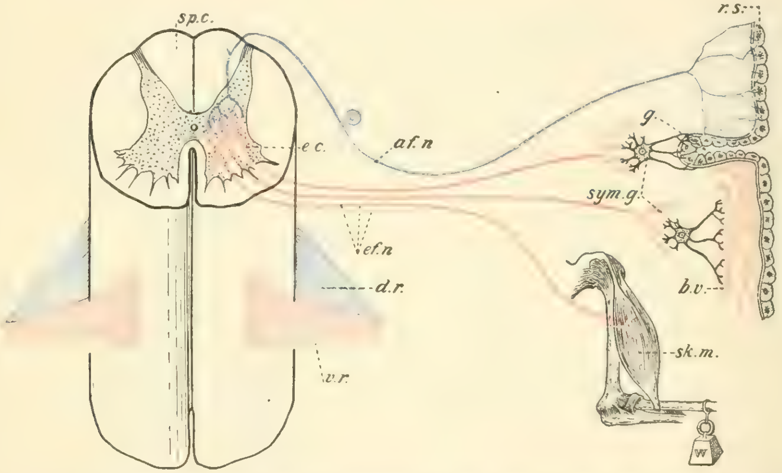

FIG. 13.—DIAGRAM SHOWING THE STRUCTURES INVOLVED IN THE PRODUCTION OF REFLEX ACTIONS.—(*G. Bachman.*) *r.s.* Receptive surface; *af.n.* afferent nerve; *e.c.* emissive or motor cells in the anterior horn of the gray matter of the spinal cord, *sp.c.; ef.n.* efferent nerves distributed to responsive organs, *e.g.*, directly to skeletal muscles, *sk.m.*, and indirectly through the intermediation of sympathetic ganglia, *sym.g.*, to blood-vessels, *b.v.*, and to glands, *g.* The nerves distributed to the walls of the viscera are not represented; *v.r.* and *d.r.*, ventral and dorsal roots and spinal nerves.

(The relation of the nerve-tissue to the skeletal muscles, to glands, to blood-vessels, and viscera are shown in Figs. 12, 13.)

The Spinal Cord.—The spinal cord is more especially the seat of origin of the nerve energy that immediately excites and controls the activity of the motor organs, and a knowledge of its structure, of its relations to these organs, and the manner in which it is, in turn, excited to activity is necessary to an understanding of the problem of movement.

The spinal cord is narrow and cylindric in shape and occupies the spinal canal from the level of the first vertebra as far down as the second or third lumbar vertebra. It presents both on its ventral and dorsal surfaces a deep longitudinal fissure which partly divide the cord into halves, a right and a left.

The Spinal Nerves.—To each side of the spinal cord there are attached thirty-one nerves, which as they pass out through foramina in the walls of the spinal column are termed spinal nerves. Each spinal nerve is connected with the spinal cord by two roots, termed from their relation to the ventral and dorsal surfaces, the *ventral* and *dorsal* roots. A short distance from the spinal cord these two roots unite to form the spinal nerve proper, after which the fibers composing it pass outward to be distributed to various peripheral organs.

A transverse section of the spinal cord shows that each half is composed externally of white matter, and internally of gray matter. The gray matter in each half is arranged in the form somewhat of a crescent united in the median line by a transverse band or commissure, the whole forming a figure resembling the letter **H**. Though varying in shape in different regions of the cord, the gray matter in all situations presents on either side an anterior or ventral and a posterior or dorsal horn (Fig. 13).

In the ventral horns of the gray matter are located large nerve-cells which gives origin to nerve-fibers; these fibers early in embryologic development become connected with structures for which they are by heredity destined. With the growth of the embryo and the development of the limbs there is a corresponding growth and development of the nerve-fibers until they attain the size characteristic of the adult. The fibers collectively constitute the ventral roots. Histologic investigation has shown that some of the ventral roots contain two groups of nerve-fibers one of large and one of small size. The fibers of large size pass forward and become *directly* connected with the skeletal muscle. The fibers of small size pass forward but for a short distance, after which they leave the ventral root and enter a group of nerve-cells (the so-called sympathetic ganglion) around the dendrites of which their terminal branches are disposed; from these cells new non-medullated fibers arise which pass backward into the spinal nerve and in association with the fibers of large size pass to vascular muscleand gland epithelium more especially of the skin and mucous membrane. In some situations the fibers of small size pass through or alongside of these ganglia to other ganglia more or less distant in which they terminate in a similar manner; from the cells of these ganglia new non-medullated nerve-fibers arise which pass directly to visceral and vascular muscles and perhaps to gland epithelium. The two portions of these nerves of small size are known respectively, as pre- and post-ganglionic.

The nerve-fibers of small size found in the ventral roots of the spinal nerves and in some of the encephalic nerves and distributed by way of the ganglia to visceral and vascular muscles and to gland epithelium constitute a system of nerves termed the *autonomic* system (see Chapter XXVI).

The dorsal root fibers originate from cells situated outside of, but derived from the spinal cord. The cells in this situation at first develop two processes from opposite ends, which at a later period shift their position, unite and form a single process after which, a division into two branches takes place, one of which passes toward and into the spinal cord and becomes related in part with the nerve-cells in the ventral horn of the gray matter, the other of which passes to the periphery and becomes connected with the skin and mucous membrane covering the surfaces of the body (Fig. 13). The surfaces of the body thus become associated anatomically and hence physiologically with the motor organs.

With the growth and development of the brain and especially of the cerebrum, nerve-cells make their appearance in the outer or cortical portion. From the cells of certain specialized regions nerve-fibers pass downward as far as the medulla oblongata, where for the most part, they cross over to the opposite side and then descend the spinal cord to give off branches or fibers at different levels which become related histologically with the nerve-cells in the ventral horns of the gray matter. The cerebrum is thus brought into relation through the intermediation of the spinal cord, with skeletal, vascular and visceral muscles and gland epithelium (Fig. 12).

Coincident with the development of the nerve-fibers descending from the cerebrum to the spinal cord, nerve-cells are developing in the more central regions of the gray matter of the spinal cord from which nerve-fibers arise that cross to the opposite side of the cord and then ascend directly or indirectly to the cerebrum where their terminal branches come into physiologic relationship with groups of specialized nerve-cells in different regions of the cortex. Of the fibers of the dorsal roots some, as previously stated, pass forward to the gray cells in the ventral horn; others, however, become associated with the more centrally located nerve-cells above alluded to. The surfaces of the body are thus brought into relationship through the intermediation of the spinal cord with the cortex of the cerebrum.

The statements, made in the foregoing paragraphs in reference to the spinal nerves, hold true for the twelve cranial nerves which correspond physiologically at least with the ventral and dorsal roots of the spinal nerves. Their relation to the cortex of the cerebrum is similar.

The nerve-fibers connecting the cerebrum with the motor organs constitute the outgoing or efferent side of the nerve system. The nerve-fibers connecting the surfaces of the body with the cerebrum constitute the ingoing or afferent portion of the nerve system.

The Efferent Spinal Nerve-cells.—It has been experimentally demonstrated that each nerve-cell in the ventral horn not only generates but under given conditions discharges a form of energy termed a *nerve impulse*, which is transmitted by the nerve-fiber arising from it and by way of the ventral roots of the spinal nerves directly to skeletal muscles and indirectly through the sympathetic ganglia and their branches to glands, blood-vessels and walls of viscera. (See Fig. 13.)

The arrival of the nerve impulse at once calls forth the form of activity characteristic of the structure stimulated. Thus the muscle, for example, passes from the passive to the active state, that is, the muscle becomes shorter and thicker, and the bone to which it is attached is moved. This is at once followed by a return of the muscle to the passive state; that is, it lengthens, becomes narrower, and resumes its original form; the bone at the same time returns to its former position. Coincident with this change of shape there is a liberation of heat and electricity. The nerve impulse which occasions this transformation of potential into kinetic energy is the normal or the physiologic stimulus. The glands in response to the nerve impulse pour out a secretion, the blood-vessels and viscera change their caliber; all these tissues responding to the nerve impulse in a characteristic manner are said to be irritable.

The nerve-cells in the ventral horns of the gray matter of the spinal cord are therefore the sources of the energy requisite for the physiologic excitation of the motor organs. If they are destroyed either experimentally or by pathologic processes, the energy is no longer discharged and the motor organs become incapable of performing their functions in a physiologic manner.

The nerve-cells, though extremely irritable, do not possess spontaneity of action, but require for their excitation the arrival and stimulating action of other nerve impulses. These may come (1) from the periphery through afferent nerve-fibers by way of the dorsal roots of the spinal nerves; and (2) from motor nerve-cells in the cortex of the cerebral portion of the brain, through descending axons or nerve-fibers.

In the first instance the resulting movements taking place in response to a peripheral or surface stimulation and independently of volitional or emotional activity are termed reflex movements; in the second instance the resulting movements taking place in response to volitional or emotional activities are termed volitional or emotional movements.

In the case of reflex movements, the nerve impulses are primarily developed in specialized organs located in the skin or mucous membranes and as a result of the impact of various external agents, which for this reason are termed *stimuli*. The nerve impulses thus developed are transmitted by the afferent nerves to the efferent or motor nerve-cells which are in turn excited to activity as a result of which, motor organs are aroused to action.

In the case of both the volitional skeletal-muscle movements and the affective or emotional viscero-muscle and vasculo-muscle movements as well as the activities of glands, the nerve impulses which cause the movements are discharged from certain motor or efferent nerve-cells in the gray matter of the cortex of the cerebrum and transmitted by descending axons or nerve-fibers direct to the nerve-cells in the spinal cord, by which they in turn are excited to activity.

The movements due to cerebral or psychic activity are, however, the immediate or the more or less remote effects of sensations which have been evoked in the sense areas of the brain, by the arrival of nerve impulses coming through ascending axons, or nerve-fibers from peripheral sense organs, *e.g.*, skin, eye, ear, nose, tongue, and which have been developed by the impact of objects in the external world.

The only organ that can be properly said to be excited to action by a volitional act is the skeletal muscle; the glands, blood-vessels, and viscera and the autonomic nerves which control them are apparently only influenced in their activity by emotional states. Why this difference should exist it is difficult to state.

The nerve-cells and their related nerve-fibers, responding by the development and conduction of nerve impulses are also said to be irritable. The transformation of energy, however, manifests itself mainly as electricity and molecular motion. The animal body in its entirety may therefore be regarded as a machine for the transformation of potential energy into kinetic energy, viz., heat and electricity, movements of muscles and bony levers, secretion, sensation and other forms of nerve activity. When muscles and bones are applied to the overcoming of opposing forces, mechanic work is accomplished. In the following chapters some of the problems connected with the activities of the primary mechanisms, the skeletal, muscle and nerve tissues will be first considered and subsequently some of the problems connected with the activities of the secondary mechanisms.

CHAPTER VI

THE PHYSIOLOGY OF THE SKELETON

The skeleton in its entirety determines the plan of organization of the animal body and imparts to it its characteristic features. In its entirety it serves for the attachment of muscles, the support of viscera and by reason of the relation of the bones one to another, permits of a great variety of movements. The skeleton may be divided into an axial and an appendicular portion.

The Axial Portion.—The axial portion consists of the bones of the head, of the vetebral column and the ribs. The vertebral column is the foundation element and the center around which the appendicular portions are developed and arranged with a certain degree of conformity. It is composed of a series of superimposed bones, the vertebræ, which increase in size from above downward as far as the brim of the pelvic cavity. Superiorly, it supports the skull; laterally, it affords attachment for the ribs, which in turn support the weight of the upper extremities; below, it rests upon the pelvic bones, which transmit the weight of the body to the inferior extremities. The bodies of the vertebræ are united one to another by tough elastic discs of fibro-cartilage, which, collectively, constitute about one-quarter of the length of the vertebral column. The vertebræ are held together by ligaments situated on the anterior and posterior surfaces of their bodies, and by short, elastic ligaments between the neural arches and processes. These structures combine to render the vertebral column elastic and flexible, and enable it to resist and diminish the force of shocks communicated to it. In all the static and dynamic states of the body it plays a most essential rôle. The character and the arrangement of the bones of the axial portion endow the animal mechanism with a certain degree of fixity combined with slight mobility.

The Appendicular Portion.—The appendicular portion consists of the bones of the arms and legs, the scapular and pelvic arches. By reason of its character and anatomic arrangement, the animal body is endowed with extreme mobility, enabling the animal to execute a great variety of rapid and extensive movements which, however, vary in degree in different animals in accordance with their organization and the nature of their environment.

For the manifestation of the activities of the animal it is essential that the relation of the various portions of the bony skeleton to one another shall be such as to permit of movement while yet retaining close apposition. This is accomplished by the mechanical conditions which have been evolved at the points of union of bones, and which are technically known as articulations or joints.

A consideration of the body movements involves an account of (1) the static conditions, or those states of equilibrium in which the body is at rest —*e.g.*, standing, sitting; (2) the dynamic conditions, or those states of activity characterized by movement—*e.g.*, walking, running, etc. In this connection, however, only those physical and physiologic peculiarities of the skeleton, especially in its relation to joints, will be referred to, which underlie and determine both the static and dynamic states of the body.

Structure of Joints.—The structures entering into the formation of joints are:

1. *Bones*, the articulating surfaces of which are often more or less expanded, especially in the case of long bones, and at the same time variously modified and adapted to one another in accordance with the character and extent of the movements which there take place.
2. *Hyaline cartilage*, which is closely applied to the articulating end of each bone. The smoothness of this form of cartilage facilitates the movements of the opposing surfaces, while its elasticity diminishes the force of shocks and jars imparted to the bones during various muscular acts. In a number of joints, plates or discs of white fibro-cartilage are inserted between the surfaces of the bones.
3. *A synovial membrane*, which is attached to the edge of the hyaline cartilage, entirely inclosing the cavity of the joint. This membrane is composed largely of connective tissue, the inner surface of which is lined by endothelial cells, which secrete a clear, colorless, viscid fluid—the synovia. This fluid not only fills up the joint-cavity, but, flowing over the articulating surfaces, diminishes or prevents friction.
4. *Ligaments*—tough, inelastic bands, composed of white fibrous tissue—which pass from bone to bone in various directions on the different aspects of the joint. As white fibrous tissue is inextensible but pliant, ligaments assist in keeping the bones in apposition, and prevent displacement while yet permitting of free and easy movements.

Classification of Joints.—All joints may be divided, according to the extent and kind of movements permitted by them, into (1) diarthroses; (2) amphiarthroses; (3) synarthroses.

A. *Diarthroses.*—In this division of the joints are included all those which permit of free movement. In the majority of instances the articulating surfaces are mutually adapted to each other. If the articulating surface of one bone is convex, the opposing but corresponding surface is concave. Each surface, therefore, represents a section of a sphere or a cylinder, which latter arises by rotation of a line around an axis in space. According to the number of axes around which the movements take place all diarthrodial joints may be divided into:

1. Uniaxial Joints.—In this group the convex articulating surface is a segment of a cylinder or cone, to which the opposing surface more or less completely corresponds. In such a joint the single axis of rotation, though nearly, is not exactly at right angles to the long axis of the bone, and hence the movements—flexion and extension—which take place are not confined to one plane. Joints of this character—*e.g.*, the elbow, knee, ankle, the phalangeal joints of the fingers and toes—are, therefore, termed ginglymi, or hinge-joints. Owing to the obliquity of their articulating surfaces, the elbow and ankle are *cochleoid* or *screw-ginglymi.* Inasmuch as the axes of these joints on the opposite sides of the body are not coincident, the right elbow and left ankle are right-handed screws; the left elbow and right ankle, left-handed screws. In the knee-joint the form and arrangement of the articulating surfaces are such as to produce that modification of a simple hinge known as a

spiral hinge, or *helicoid*. As the articulating surfaces of the condyles of the femur increase in convexity from before backward, and as the inner condyle is longer than the outer, and, therefore, represents a spiral surface, the line of translation or the movement of the leg is also a spiral movement. During flexion of the leg there is a simultaneous inward rotation around a vertical axis passing through the outer condyle of the femur; during extension a reverse movement takes place. Moreover, the slightly concave articulating surfaces of the tibia do not revolve around a single fixed transverse axis, as in the elbow-joint, for during flexion they slide backward, during extension forward, around a shifting axis, which varies in position with the point of contact.

In some few instances the axis of rotation of the articulating surface is parallel with, rather than transverse to the long axis of the bone, and as the movement takes place around a more or less conic surface, the joint is termed a *trochoid* or pulley—*e.g.*, the odonto-atlantal and the radio-ulnar. In the former the collar formed by the atlas and its transverse ligament rotates around the vertical odontoid process of the axis. In the latter the head of the radius revolves around its own long axis upon the ulna, giving rise to the movements of pronation and supination of the hand. The axis around which these two movements take place is continued through the head of the radius to the styloid process of the ulna.

2. Biaxial Joints.—In this group the articulating surfaces are unequally curved, though intersecting each other. When the surfaces lie in the same direction, the joint is termed an *ovoid* joint—*e.g.*, the radio-carpal and the atlanto-occipital. As the axes of these surfaces are vertical to each other, the movements permitted by the former joint are flexion, extension, adduction, and abduction, combined with a slight amount of circumduction; the latter joint permits of flexion and extension of the head, with inclination to either side. When the surfaces do not take the same direction, the joint, from its resemblance to the surfaces of a saddle, is termed a saddle-joint—*e.g.*, the trapezio-metacarpal. The movements permitted by this joint are also flexion, extension, adduction, abduction, and circumduction.

3. Polyaxial Joints.—In this group the convex articulating surface is a segment of a sphere, which is received by a socket formed by the opposing articulating surface. In such a joint, termed an *enarthrodial* or ball-and-socket joint—*e.g.*, the shoulder-joint, hip-joint—the distal bone revolves around an indefinite number of axes, all of which intersect one another at the center of rotation. For simplicity, however, the movement may be described as taking place around axes in the three ordinal planes—viz., a transverse, a sagittal, and a vertical axis. The movements around the transverse axis are termed flexion and extension; around the sagittal axis, adduction and abduction; around the vertical axis, rotation. When the bone revolves around the surface of an imaginary cone, the apex of which is the center of rotation and the base the curve described by the hand, the movement is termed circumduction.

B. *Amphiarthroses*.—In this division are included all those joints which permit of but slight movement—*e.g.*, the intervertebral, the interpubic, and the sacro-iliac joints. The surfaces of the opposing bones are united and held in position largely by the intervention of a firm, elastic disc of fibro-cartilage. Each joint is also strengthened by ligaments.

C. *Synarthroses.*—In this division are included all those joints in which the opposing surfaces of the bones are immovably united, and hence do not permit of any movement—*e.g.*, the joints between the bones of the skull.

Levers.—In the animal machine, as in physical machines generally, work is accomplished by the intermediation of levers. The bones collectively constitute a system of levers the fulcra of which lie in the joints. The long bones more especially, are the levers which are employed by the muscles to overcome the opposing forces or resistances. The structure and the chemic composition of the bones, consisting as they do of inorganic matter 67 per cent. and of organic matter 33 per cent. endow them with both rigidity and elasticity, physical properties which admirably adapt them to the character of the work necessitated by the environment and the organization of the animal. The rigidity of bone is considerable as compared with other hard and rigid materials. The breaking limit, in terms of the weight in kilos required to tear across a rod 1 square millimeter in cross-section of various materials is as follows: Cast iron 13; bone 12; oak 6.5; granite 1.9. The elasticity is about one-sixth that of wrought iron and twice that of oak parallel to the grain (MacAlister). In youth bones are quite elastic; in old age they are fragile because of a diminution of osseous tissue and an increased porosity, and, therefore, at both periods less capable of functionating as effectively as in the middle period of life. The animal body presents many illustrations of the three orders of levers, their advantages and disadvantages from the mechanical point of view.

The nature of the opposing forces, however, is of such a character that the animal and especially man, is but to a slight degree capable of overcoming them with the natural anatomic and physiologic levers. With the invention of tools (physical levers) of all kinds and their utilization by man the effectiveness of the anatomic levers in the performance of work has been enormously increased. Through their coöperation the progress of man in the arts of civilization has been made possible.

The axial portion of the skeleton possesses largely, joints of the amphiarthrodial character which endow the vertebral column with certain forms of movement which are necessary to the performance of many body activities. While the range of movement between any two vertebræ is slight, the sum total of movement of the entire series of vertebræ is considerable. In different regions of the column the character, as well as the range of movement, varies in accordance with the form of the vertebræ and the inclination of their articular processes. In the cervical and lumbar regions extension and flexion are freely permitted, though the former is greater in the cervical, the latter in the lumbar region, especially between the fourth and fifth vertebræ. Lateral flexion takes place in all portions of the column, but is particularly marked in the cervical region. A rotatory movement of the column as a whole takes place through an angle of about twenty-eight degrees. This is most evident in the lower cervical and dorsal regions.

The appendicular portion possesses largely, joints of the diarthrodial character which permit of free movement. The character of the movement depends mainly on the shape and adjustment of the bones at their points of union.

CHAPTER VII

GENERAL PHYSIOLOGY OF MUSCLE-TISSUE

The Muscle-tissue.—The muscle-tissue, which closely invests the bones of the body and which is familiar to all as the flesh of animals, is the immediate cause of the active movements of the body. This tissue is grouped in masses of varying size and shape, which are technically known as muscles. The majority of the muscles of the body are attached to the bones of the skeleton in such a manner that, by an alteration in their form, they can change not only the position of the bones with reference to one another, but can also change the individual's relation to surrounding objects. They are therefore, the active organs of both motion and locomotion, in contradistinction to the bones and joints, which are but passive agents in the performance of the corresponding movements. In addition to the muscle masses which are attached to the skeleton, there are also other collections of muscle-tissue surrounding cavities such as the stomach, intestine, blood-vessels, etc., which impart to their walls motility, and so influence the passage of material through them.

Muscles produce movement of the structures to which they are attached by the property with which they are endowed of changing their shape, shortening or contracting under the influence of a stimulus transmitted to them from the nerve system. Muscles are divided into:

1. *Skeletal* muscles, comprising those muscles which are attached to the various bones of the skeleton.
2. *Visceral* muscles, comprising those muscles which are found in and which compose a portion of the walls of the hollow viscera.

As the skeletal muscles are capable of being excited to activity by nerve impulses descending from the cerebrum as a result of volition they are frequently termed voluntary muscles. By reason of their appearance as seen under the microscope they are termed also striped or striated muscles. As the visceral muscles are not capable of being excited to action by volition they are frequently termed involuntary muscles. By reason of their appearance as seen under the microscope they are termed also non-striated or smooth muscles.

Though for the most part the skeletal muscles are *red* in color, there are certain muscles in man and other animals which are *pale* in color and in many muscles, pale fibers are extensively distributed among the red fibers.

THE SKELETAL OR VOLUNTARY MUSCLE

All skeletal muscles consist of a central fleshy portion, the body or belly, provided at either extremity with a tendon in the form of a cord or membrane. The body is the active, contractile region, the source of the movement; the tendon is the inactive region, the passive transmitter of the movement to the bones.

A skeletal muscle is a complex organ consisting of a framework of connective tissue, supporting muscle-fibers, blood-vessels, nerves, and lymphatics. The general body of the muscle is covered by a dense layer of connective tissue, the epimysium, which blends with and partly forms the tendon. From the under surface of this covering, septa of connective tissue pass inward, dividing and grouping the fibers into larger and smaller bundles, termed fasciculi. The fasciculi, invested by a special sheath, the perimysium, are prismatic in shape and on cross-section present an irregular outline. The muscle-fibers composing the fasciculi are separated one from another and supported by a very delicate connective tissue, the endomysium. The connective tissue thus surrounding and penetrating the muscle binds the fibers into a distinct organ and affords support to all remaining structures (Fig. 14).

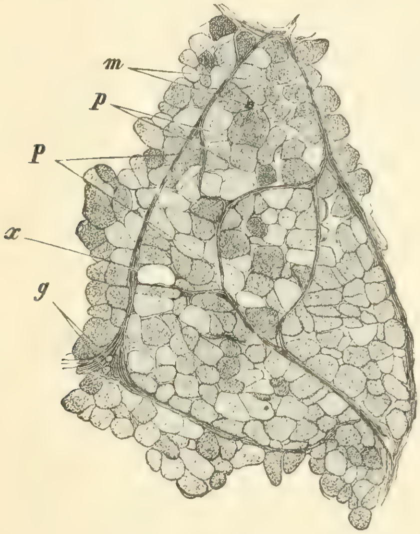

FIG. 14.—FROM A CROSS-SECTION OF THE ADDUCTOR MUSCLE OF A RABBIT. *P*. Perimysium, containing two blood-vessels, at *g*; *m*, muscle-fibers; many are shrunken and between them the endomysium, *p*, can be seen; at *x* the section of muscle-fiber has fallen out. × 60.—(*Stöhr*.)

Histology of the Skeletal Muscle-fiber.—The muscle-fiber is the ultimate anatomic unit of the muscle system. The fibers for the most part are arranged parallel one to another and in a direction corresponding to the long axis of the muscle. They vary in length from 30 to 40 millimeters and in breadth from 20 to 30 micromillimeters. There are exceptional fibers, however, which have a much greater length. As the fibers have but a limited length in the vast majority of muscles, each end, more or less pointed or beveled, is united to adjoining fibers by cement. In this way the length of the muscles is built up.

When examined with the microscope, the muscle-fiber is seen to be cylindric or prismatic in shape and to consist of a thin transparent membrane, the sarcolemma, in which is contained the true muscle substance or sarcous substance. The sarcolemma is elastic and adapts itself to all changes of form the sarcous substance undergoes. Beneath the sarcolemma there are several nuclei surrounded by granular material; a muscle-fiber may therefore be regarded as a large multinucleated cell. Each fiber also presents a series of transverse bands alternately dim and bright which give to it a striated appearance. If the bright bands are examined with high magnifying powers, each one is seen to be crossed by a fine dark line which at the time of its discovery by Krause was regarded as the optic expression of a membrane attached laterally to the sarcolemma. According to Rollet, it is composed of a series of granules so closely applied as to give rise to the appearance of a continuous line (Fig. 15).

The muscle-fiber also presents a longitudinal striation which indicates that it is composed of finer elements placed side by side, termed fibrillæ. The fibrillæ extend throughout the entire length of the fiber, though they are not of uniform thickness. That portion of the fibrilla corresponding in position to the dim band is thick, prismatic, or rod-like in shape, and termed a sarcostyle; that portion corresponding in position to the bright band is extremely thin and narrow and presents at its middle a slight enlargement or nodule. The fibrillæ are embedded in a clear transparent fluid which, from its supposed nutritive character, is termed sarcoplasm, or interfibrillar substance. The diminution in caliber of the fibrillæ at different levels would permit of the accumulation and storage of a larger amount of this nutritive material than could otherwise be the case. It is for this reason that the fiber at these points presents a brighter appearance.

When the muscle-fiber is examined by polarized light, the dim band appears bright and the bright band appears dim against a dark background, indicating that the former is doubly refracting or anisotropic, the latter singly refracting or isotropic.

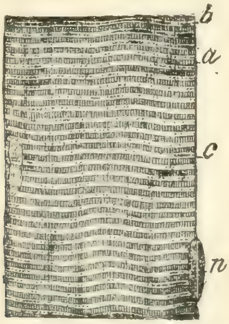

Fig. 15.—Muscle-fiber of a Rabbit. *a.* Dark band. *b.* Light band. *c.* Intermediate line. *n.* Nucleus.—(*Landois and Stirling.*)

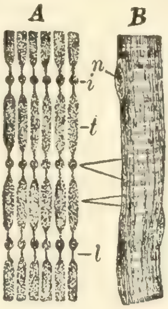

Fig. 16.—*A.* Diagram of arrangement of the contractile substance according to the view of Rollett; the granular figures represent the contractile elements, the intervening light areas the sarcoplasm. *B.* Small muscle-fiber of man; the corresponding parts in the two figures are indicated; *t*, *i*, *l*, respectively the transverse, the intermediate, and lateral discs. *n.* Muscle nuclei.—(*Piersol.*)

This interpretation of the structure of the muscle-fiber has been subjected to criticism in recent years by Heidenhain. This observer regards the transverse line in the bright band as did its discoverer Krause as a true membrane which is attached laterally to the sides of the sarcolemma. The fibrillæ he also regards as continuous but of uniform thickness, and passing directly through the transverse membrane by which they are supported and maintained in their normal relation. In this view the fibrilla consists of alternate regions of a doubly refracting and a singly refracting material. The sarcoplasm is, therefore, confined to the interfibrillar spaces. Fig. 17.

The fiber of the pale muscle is similar histologically to the fiber of the red muscle. It, however, does not contain so much granular protoplasm as does the fiber of the red muscle and hence does not intercept the light to the same extent. The greater the quantity of granular protoplasm the darker the muscle.

The Blood-supply.—Muscles in the physiologic condition require for the maintenance of their activity a large amount of nutritive material. This is obtained directly from the lymph and indirectly from the blood furnished by the blood-vessels. The vascular supply to the muscles is very great and the disposition of the capillary vessels with reference to the muscle-fiber is very characteristic. The arterial vessels, after entering the muscle, are supported by the peri-mysium; in this situation they give off short transverse branches, which immediately break up into a capillary network of rectangular shape within which the muscle-fibers are contained.

The muscle-fiber, in intimate relation with the capillary, is bathed with lymph derived from it. Its contractile substance, however, is separated from the lymph by its own investing membrane, through which all interchange of nutritive and waste material must take place.

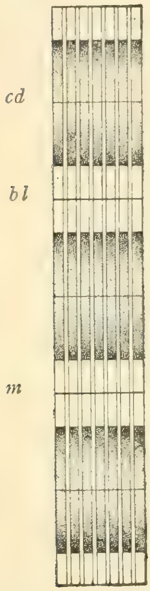

FIG. 17.—DIAGRAM OF MUSCLE STRIATIONS.—(*Modified from "Stönr's Histology.*") The fibrillæ consists of alternate dark bands, *d.b.*, and light bands, *l.b.* *l.b.* is crossed by Krause's membrane, *m.*; a similar membrane crosses the dim band according to Heidenhain.

The nutritive material passes through the capillary wall into the lymph-space, then through the sarcolemma into the interior of the fiber, where it comes into relation with the living muscle material. The waste products arising in the muscle as a result of nutritive changes pass in the reverse direction first into the lymph and then into the blood, by which they are carried away to eliminating organs. Lymphatics are present in muscle, but confined to the connective tissue, in the spaces of which they take their origin.

The Nerve-supply.—The nerves which carry the stimuli to a muscle enter near its middle point. Many of the fibers pass directly to the muscle-fibers with which they are connected; others are distributed to blood-vessels. Every muscle-fiber is supplied with a special nerve-fiber except in those instances where the nerve-trunks entering a muscle do not contain as many fibers as the muscle. In such cases the nerve-fibers divide near their termination until the number of branches equals the number of muscle-fibers. The individual muscle-fiber is penetrated near its center by the nerve where it terminates; the ends being practically free from nerve influence. The stimulus that comes to the muscle-fiber acts primarily upon its center, the effect of which then travels in both directions to the ends. The manner in which the nerve-fibers terminate in muscle will be more fully described in connection with the histology of the nerve-tissue.

CHEMIC COMPOSITION OF MUSCLE

The chemic composition of living muscle is but imperfectly understood owing to the fact that shortly after death some of its constituents undergo a spontaneous coagulation and for the reason that the methods employed for analysis also tend to alter its composition. To human muscle, the following average percentage composition has been given:

Water	73.5	
Proteins, including those of sarcolemma, connective tissue, pigments	18.02	
Gelatin	1.99	
Fat	2.27	
Extractives	0.22	
Inorganic salts	3.12	(Halliburton.)

When fresh muscle is freed from fat and connective tissue, frozen, rubbed up in a mortar, and expressed through linen, a slightly yellow syrupy alkaline or neutral liquid is obtained which has been termed muscle-plasma. This fluid at normal temperatures coagulates spontaneously, the phenomena resembling in many respects those observed in the coagulation of blood-plasma. The coagulum subsequently contracts and squeezes out an acid muscle-serum. The coagulated protein partakes of the nature of fibrin and belongs to the class of globulins. Inasmuch as it is not present in living muscle and only makes its appearance under conditions not strictly physiologic, it is regarded as a derivative of pre-existing proteins. An analysis of muscle-plasma has shown the presence of at least two proteins which are distinguished by their varying solubilities in different salt solutions, and by the varying temperatures at which they coagulate. One of these proteins coagulates at about 47°C. and because of its chemic relations has been termed myosin or paramyosinogen; the other coagulates at about 56°C. and for similar reasons has been termed myogen or myosinogen. The latter is three or four times more abundant than the former. If the temperature of the cooled plasma be permitted to rise, both myosin and myogen undergo a change of state termed coagulation. The substances resulting are known as myosin fibrin and myogen fibrin. It is not known whether these changes are due to the action of an enzyme or not. A similar change in myosin and myogen occurs after death, giving rise to the condition known as death stiffening or rigor mortis. The coagulation of these proteins in this instance is probably caused by the presence and accumulation of metabolic products. From the muscle-serum, according to Halliburton, may also be obtained at 68°C. a globulin body termed myoglobulin and a small quantity of myo-albumin. Among the proteins may be mentioned hemoglobin, which gives the color to the muscles. Spectroscopic investigation reveals the presence of a special pigment, myohematin, which is supposed to have a respiratory function, inasmuch as its spectral absorption bands change by oxidation and reduction.

Among the extractives containing nitrogen may be mentioned creatin, creatinin, xanthin, carnin, urea, uric acid, carnic acid, etc. Among the extractives free of nitrogen, glycogen, dextrose, inosite, lactic acid and fat, are the most important. Inorganic salts are relatively abundant, of which potassium is the most abundant among the bases, and phosphoric acid among the acids.

THE PHYSICAL AND PHYSIOLOGIC PROPERTIES OF MUSCLE-TISSUE

Consistency.—The consistency of muscle-tissue during life varies considerably in accordance with different states of the muscle. In a state of tension it is hard and resistant; in the absence of tension it is soft and fluctuating to the sense of touch. Tension alone gives rise to hardness.

Cohesion.—The cohesion of a muscle is largely dependent on the quantity of connective tissue it contains. A band of fresh human muscle 1 square centimeter in cross-section has been found able to resist a weight of 14 kilograms without rupture (MacAlister). Cohesion resists the forces of traction and pressure.

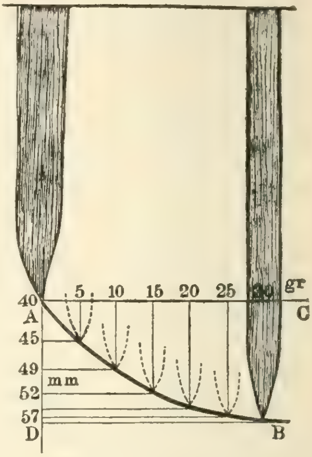

Fig. 18.—Extension Curve of Muscle.—(*Gad.*)

Elasticity.—Muscle, in common with many other organic as well as inorganic substances, is capable of being extended beyond its normal length by the action of external forces and of resuming the normal length when these forces cease to act. All such bodies are said to be elastic; and the greater the variations between the natural and acquired lengths, the greater is their elasticity said to be. Muscles, therefore, possessing extensibility and retractility are said to be elastic. If the muscle of a frog, preferably the sartorius, the fibers of which are arranged in a practically parallel manner, be fastened at one extremity by a clamp, and then extended by a series of successive weights which differ by a common increment, it will be found that the extensibility of muscle does not follow the law of elasticity as determined for inorganic bodies; *i.e.*, directly proportional to the weight and to the length of the body extended; but that while increasing in length with each successive weight, the increase is always in a diminishing ratio. Thus, for example, as shown in Fig. 18: The extension produced by 5 grams is 5 millimeters, that produced by 10 grams is only 4 millimeters more, and so on with additional weights until the increase in passing from 25 to 30 grams is only 1 millimeter. The extensibility is thus shown to be proportionately greater with small than with larger weights. It is, however, actually greater with the larger weights. The extension curve A B formed by joining the ends of the muscle approximates that of a parabola. The behavior of the muscle in returning to its original length also shows a variation from the behavior of inorganic bodies. With the successive removal of the weights, the elasticity of the muscle asserts itself with gradually increasing energy until its normal length is nearly, if not entirely, regained (Fig. 19). It is usually stated that the elasticity of muscle is incomplete, but it must be borne in mind that the experiments have usually been made on muscles removed from the body, deprived of blood and nerve influences, and hence under abnormal conditions. It is highly probable that in the living body muscles possess perfect elasticity which enables them completely to return to their normal length after extension. The extension and retraction or elastic recoil of muscle depends on the maintenance of physiologic conditions. If the nutrition is impaired by fatigue,

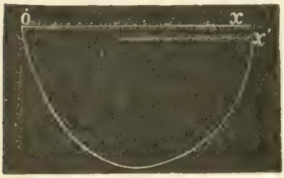

Fig. 19.—Curve of Elasticity Produced by Continuous Extension and Recoil of a Frog's Muscle. *o x*. Abscissa before; *x'*, after extension.—(*Landois and Stirling.*)

deficient blood-supply, or any pathologic condition, the elasticity is at once impaired.

Tonicity.—Muscle tonus may be defined as a state of tension of a muscle due to a slight but continuous contraction of its individual fibers in consequence of which it tends to become shorter, and would do so, were it not restrained by its attachments. As a result of this tension its efficiency as a quickly responsive motor organ is increased. Though the skeletal musculature of the body as a whole is in a state of tonus, individual muscles vary in the degree of their tonus from time to time in consequence of variations in the causes that give rise to it. That such a tonus or tension exists is apparently shown by the fact that when a muscle in a living animal is divided the two portions will retract and separate a certain distance. This would indicate that the muscle even in a state of relative rest is in a slight degree of contraction.

This condition of tonus is attributed to the continuous arrival of nerve impulses through efferent nerves discharged by nerve-cells in the spinal cord. The tonus was therefore at one time attributed to an automatic activity of the spinal cord. Brondgeest, however, showed that this was not the case, but that the activity of the spinal cord and hence the tonus of the muscles is partly reflex in origin inasmuch as it largely disappears on division of the posterior or dorsal roots of the spinal nerves. The afferent impulses exciting the cord reflexly may come from the skin in which they are developed by the impressions made by external stimuli, or from the tendons and muscles themselves in which they are developed by the slight degree of extension and variations in extension to which these are subjected from moment to moment. That this latter is a considerable factor in the production of the tonus is shown by the effects which follow division of the afferent nerves coming from any given muscle group; with the division of the nerves the muscles relax and lose their usual tone. It is also probable that the activity of the cord is partly the result of impulses descending the cord in consequence of cerebral and sense organ activities.

Muscle tonus or elastic tension plays an important rôle in muscle contraction; being always on the stretch the muscle loses no time in acquiring that degree of tension necessary to immediate action on the bone to which it is attached. The working power of a muscle is also considerably increased by the presence within limits of some resistance to the act of contraction. According to Marey, the amount of work is considerably increased when the muscle energy is transmitted by an elastic body to the mass to be moved, while at the same time the shock of the contraction is lessened. The position of a passive limb is the resultant also of the elastic tension of antagonistic groups of muscles. Again as a result of the slight but continuous stimulation from the spinal cord the metabolic changes in the muscle material are maintained at a certain level, with a corresponding production of heat. A function of the tonicity would thus be the production of heat, other functions which the tone subserves being more or less secondary.

Irritability, Contractility.—These are terms employed to denote that property of muscle-tissue by virtue of which it responds by a change of form, becoming shorter and thicker on the application of a stimulus. On the withdrawal of the stimulus the muscle again undergoes a reverse change of form, becoming longer and narrower, and returning to its original condition. All muscles which possess this capability are said to be irritable and contractile; and all agents which call forth this response of the muscle are termed stimuli. The rapid change of form which a highly irritable muscle undergoes in response to the action of a stimulus of short duration is usually termed a twitch or pulsation. With appropriate apparatus it can be shown that the muscle at the time of the twitch becomes warmer and exhibits electric phenomena. The muscle is therefore an apparatus for the conversion of potential into kinetic energy: viz., heat, electricity, and mechanic motion.

Though usually associated with the activity of the nerve system, and to some extent dependent on it, irritability is nevertheless an independent endowment of the muscle and persists for a longer or shorter period, as shown by many experiments, after all nerve connections have been destroyed. Among the proofs which may be presented in support of this view are the following: The introduction of the drug, curara, into the body of an animal produces in a short time complete paralysis. Experiment has shown that curara suspends the conductivity of the intramuscular terminations of the nerve-fiber and thus separates the muscle entirely from the nerve. Though the animal is incapable of executing a single movement, its muscles respond promptly on the application of a stimulus. Moreover, portions of muscles exhibit irritability although containing no trace of nerve structure. This is the case with the ends of the sartorius muscle of the frog and the anterior end of the retractor muscle of the eyeball of the cat. These and other facts demonstrate the independence of muscle irritability.

In the living body nutritive activity and irritability are maintained by a due supply of oxygen, and of nutritive material, the removal of waste products, and a normal temperature. The muscles of the cold-blooded animals, for example the frog, retain their irritability for a much longer period after death than the muscles of the warm-blooded animals. This is the case also with the individual muscles after removal from the body of the animal. The reason for this is found in all probability in the difference in the rate of their nutritive activities and in the quantity of nutritive material stored up in their cells. The duration of the irritability of isolated muscles can be considerably prolonged by keeping them in a moist atmosphere.

Conductivity.—All muscle protoplasm possesses conductivity. The change excited in a muscle-fiber by the arrival of a nerve impulse is at once conducted with great rapidity in opposite directions to the ends of the fiber; the advance of the excitation process is immediately succeeded by the contraction process, the change of form which constitutes the contraction. With the disappearance of the former, the latter also disappears and the muscle resumes its previous passive condition. There is no evidence, however, that the excitation process travels transversely—that is, into adjoining fibers—being prevented from doing so by the presence of the limiting membranes, the sarcolemmata. The fact that each muscle-fiber receives its own, or at least a branch of a nerve-fiber, and hence its own nerve impulse or stimulus, would also indicate that the excitation process cannot be conducted longitudinally into adjoining fibers, or at least with sufficient rapidity for the purposes of ordinary muscle actions. Nevertheless if a long muscle, such as the sartorius, from a curarized frog be stimulated at one end with an induced electric current, the excitation and the contraction processes will be conducted with extreme rapidity to the opposite end of the muscle. The rapidity of conduction in human muscles has been estimated at from 10 to 13 meters per second, and in frog's muscle at from 3 to 4.5 meters per second. The contraction process, the thickening of the muscle, is termed the *contraction wave*. As it is the result of the excitation process and immediately succeeds it, its rate of conduction must be the same as that given above. With appropriate apparatus the duration of the wave at any given point has been shown to be, in the frog's muscle, about one-tenth of a second and its length three-tenths of a meter.

Muscle Stimuli.—Though consisting of a highly irritable tissue, muscles do not possess spontaneity of action. They require for the manifestation of their characteristic activity the application of a stimulus. In the living body all contractions, at least of the skeletal muscles, occurring under normal or physiologic conditions are caused by the action of "nerve impulses" transmitted by the nerves from the central nerve system to the muscles. The nerve impulse is the normal or physiologic stimulus. After removal from the body and freed from nerve connections muscles can be excited to action by various agents of a mechanic, chemic, thermic, or electric nature. These are artificial or non-physiologic stimuli.

1. *Mechanic Stimuli.*—Cutting, pinching, sharply tapping the muscle will cause it to contract, providing the stimulus has sufficient intensity. With each stimulation a short, fleeting contraction ensues. If repeated with sufficient rapidity, a series of continuous but irregular pulsations are produced.
2. *Chemic Stimuli.*—Various chemic substances in solution will excite single or continuous pulsations if the strength of the solution is not such as to destroy at once the irritability. They owe their efficiency as stimuli to the rapidity with which they alter the composition of the muscle-substance. Among these may be mentioned solutions of potassium and sodium salts, weak solutions of the mineral and organic acids, ammonium vapor, distilled water, glycerin, and sugar.
3. *Thermic Stimuli.*—The application of a heated object, such as a hot wire, causes the muscle to contract rapidly.
4. *Electric Stimuli.*—The most efficient stimulus and the one least injurious to the tissue is the electric current. Either the constant or the induced current may be used.[1]

The Constant Current.—If the ends of the wires in connection with an electric cell be provided with non-polarizable electrodes and the latter placed on opposite ends of a freshly prepared sartorius muscle of a frog which has been previously curarized, it will be found on closing or making the circuit that the muscle will exhibit a short, quick pulsation. During the actual passage of the current, especially if it is weak, there may be no apparent change in the muscle. If the current is strong, the muscle may, on the contrary, remain in a state of continuous contraction. With the opening or breaking of the current the muscle at once relaxes, or perhaps again contracts and then relaxes. The extent of the contraction depends mainly on the strength of the current, being greater with strong, less with weak currents.

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[1] Since the study of the physiologic properties of both muscle-tissue and nerve-tissue involves the employment of electricity as a stimulus, it is necessary for the student to familiarize himself with certain forms of apparatus by which it is generated, controlled, and applied. To avoid interrupting the continuity of the text this information is embodied in an appendix. The facts therein contained should be mastered at this time by the student.

When the current is sufficiently strong to elicit both making and breaking contractions, it is found that the contraction occurring on the make or closure of the circuit is regularly greater than that occurring on the break or opening of the circuit. Moreover, it has been shown in many ways that the contraction occurring on the closure of the circuit has its origin at the point where the current is leaving the muscle—*i.e.*, in the immediate neighborhood of the negative pole or cathode—and propagates itself to the opposite extremity; while the contraction occurring on the opening of the circuit has its origin at the point where the current is entering the muscle, *i.e.*, in the neighborhood of the positive pole or anode.

These facts can be readily demonstrated by destroying the irritability and contractility of one extremity of a muscle with parallel fibers such as the sartorius. On applying non-polarizable electrodes to the muscle as in Fig. 20, A, it will be found that when the circuit is made a contraction occurs which must, of course, have developed at the irritable cathodic region, for on the break of the circuit the muscle remains at rest. When the electrodes are applied as in Fig. 20, B, and the circuit made the muscle remains at rest, but on the break of the circuit a contraction occurs which must have developed at the irritable anodic region.

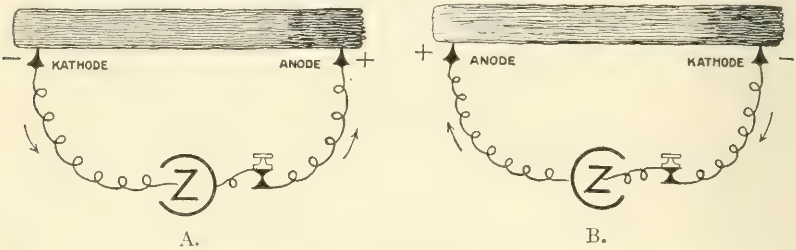

Fig. 20.—Diagram to Show the Effect of Local Injury on the Irritability of a Muscle.—(*After Starling.*) C Z an electric cell from which wires pass to non-polarizable electrodes, anode and kathode, in contact with a muscle, the injured end of which is more deeply shaded. The arrows indicate the direction of the current.

The Induced Current.—If the primary coil of the inductorium be connected with an electric cell and the secondary coil be connected with a muscle, it will be found that the current induced in the secondary circuit, both on the make and break of the primary, will also cause the muscle to pulsate sharply and rapidly if the two coils are sufficiently near each other. Observation, however, makes it evident that the pulsation occurring with the break of the primary circuit is more energetic than that occurring with the make, a result the opposite of that obtained with the constant current. This is not due to any difference in the electricity, however, but to peculiarities in the construction of the inductorium. When the primary circuit is interrupted with sufficient frequency, as it can be by throwing into the circuit Neef's hammer or some other form of interrupter, the contractions excited by the induced currents may be made to succeed one another so rapidly that they become fused together, producing a *spasm* or *tetanus* of the muscle. The rapidity with which the induced current appears and disappears, its brief duration, the ease with which its strength can be regulated, combine to render it a most efficient stimulus for either muscle or nerve.

PHENOMENA FOLLOWING A MUSCLE STIMULATION
PHYSICAL PHENOMENA

Physiologic investigation has made it apparent that when a nerve impulse reaches a muscle, it occasions a disruption of certain complex energy-holding compounds and their subsequent oxidation to simpler compounds. Coincidently with the chemic changes there is a transformation of the potential energy of the molecules into kinetic energy which manifests itself under three forms, heat, electricity and mechanic motion, or a change of shape of the muscle. These phenomena vary in extent in accordance with the intensity of the impulse as well as the frequency of its repetition. Though the chemic changes are the first effects of the action of the nerve impulse and the ones on which other phenomena depend, it will be found convenient to consider the most evident effect, the physical change in the shape of the muscle, first.

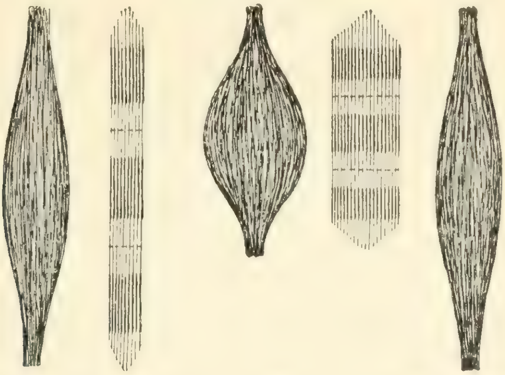

Fig. 21.—Showing the Changes in a Muscle and Muscle-fiber during Contraction.

Change of Shape.—The most obvious change in a muscle following the arrival of a nerve impulse is that relating to its form. The muscle not only becomes shorter, but at the same time thicker. The extent to which it may shorten when unopposed may amount to 30 per cent. or more of its original length. The increase in thickness practically compensates for the diminution in length, for there is no observable diminution in volume. The change in form of the entire muscle results from a corresponding change of form of its individual fibers as determined by microscopic examination, each of which becomes shorter and thicker. The successive changes in both the muscle and the individual fibers are represented in Fig. 21.

When the contraction begins both the dim and bright bands diminish in length, but at the same time increase in breadth. This continues until the contraction reaches its maximum. The diminution in the length of the bright band is greater proportionally than the diminution in the length of the dim band, a fact which gave rise to the supposition on the part of Englemann that there is at the time of the contraction a passage of fluid material from the bright into the dim band or from the sarcoplasm into the sarcostyles. When the relaxation begins, a reverse change in the dim and bright bands sets in and continues until they regain their former shape and volume. Coincidently there is a passage of fluid material from the sarcostyles to the sarcoplasm. As the contraction wave reaches its maximum the optic properties of the bright and dim bands change. The former now becomes darker and less transparent until at the crest of the wave it assumes the appearance of a distinct dark band; the latter now becomes clear and bright in comparison. This change in the appearance of the fiber is due to an increase in refrangibility of the bright, and a decrease in the refrangibility of the dim band, coincident with the passage of the fluid from the former into the latter. There is at the height of the contraction a complete reversal in the positions of the striations. At a certain stage between the beginning and the crest of the wave the striæ almost entirely disappear, giving to the fiber an appearance of homogeneity. There is, however, no change in refractive power as shown by the polarizing apparatus. When the contraction wave has reached the stage of greatest intensity, there is a reversal of the above phenomena as the fiber returns to its former condition, that of relaxation.

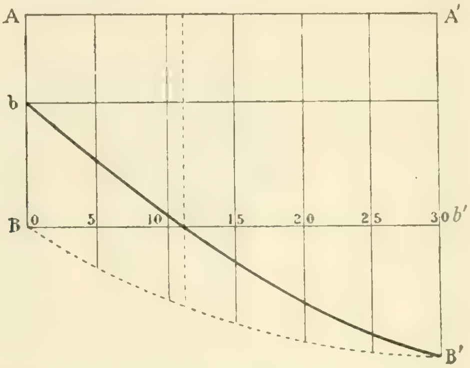

FIG. 22.—EXTENSION CURVES: B B′, of the resting; b B′, of the contracting muscle.

Change of Elasticity.—During the contraction of a muscle there is a greater or less alteration in its elasticity, as shown by the fact that it is extended to a greater degree by the same weight in the active than in the passive condition. The degree to which the extensibility is increased and the elasticity decreased is dependent on the amount of the resisting force. These facts, as determined experimentally, are represented in Fig. 22. Let A B and A b represent the length of the normal unweighted muscle, in passive and active states respectively; the line B B′, the extension curve of the passive muscle produced by successive weights, 5, 10, 15, 20, 25, 30 grams, differing by a common increment; the line b B′, the extension curve of the active contracted muscle when weighted with the same weights; A′ B′ the length of the muscle when the weight is sufficiently great to prevent shortening. It will be observed from these facts that while the muscle is extended in both the passive and active states by corresponding weights, the extension during the latter is progressively greater, until with a given weight the length of the muscle is the same. Under such circumstances, there being no shortening of the muscle, the force of its contraction manifests itself physically simply as tension. In the successive actions of the muscle represented in the same figure there is to be observed also a combination of a change of length and a change of tension, the ratio of the one to the other being determined by the amount of the supported weights. When the weight is slight in amount, the shortening of the muscle reaches a maximum and the tension a minimum; when the weight is large in amount, the reverse conditions obtain.

GRAPHIC REPRESENTATION OF THE CHANGE OF SHAPE

The contraction of a muscle as it takes place in the living body and under normal physiologic conditions is a complex act persisting for a variable length of time in accordance with the number of stimuli transmitted to it in a given unit of time, and as determined experimentally is the resultant of the fusion of a greater or less number of separate and individual contractions or pulsations. To this enduring contraction the term *tetanus* has been given. With the aid of appropriate apparatus it has become possible to obtain and record single muscle contractions, to analyze and decompose them into their constituent elements, or to combine them in such a manner as to produce practically a normal physiologic tetanus. As in the experimental study of the phenomena of muscle contraction it frequently becomes necessary to remove the muscle from the body of the animal, the muscles of warm-blooded animals are not well adapted for this purpose, owing to the rapid alteration in composition they undergo, with a consequent loss of irritability, when deprived of their normal blood-supply. The excised muscles of cold-blooded animals, such as the frog—in which, owing to the relatively slow rate of the nutritive activities, the irritability and contractility endure for a relatively long period of time, even though deprived of blood—are particularly valuable for experimental studies. The muscles generally employed are the gastrocnemius, the sartorius, and the hyoglossus. If kept at a normal temperature and moistened with 0.6 per cent. solution of sodium chlorid, such a muscle will contract for a long period of time on the application of any form of stimulus, but especially the electric.

Method of Recording a Muscle Contraction.—Inasmuch as the changes in the form of a muscle during a single contraction take place with extreme rapidity, their succession, peculiarities, and time relations cannot be determined with any degree of accuracy by the unaided eye. This difficulty can largely be overcome by the employment of the graphic method, the principle of which consists in recording the movements by means of a pen on some appropriate moving and receiving surface. To accomplish this object the muscle is attached at one extremity by a clamp to a firm support, and at the other extremity to a weighted lever, which is, however, sufficiently light to enable it to take up, reproduce, and magnify its movements. The end of the lever provided with a point is applied to a smooth surface, such as glazed paper on a cylinder or plate, covered with lampblack. If the surface is stationary, the contraction is recorded as a vertical line; if it is put in movement at a uniform rate by clockwork, the contraction is recorded in the form of a curve, the width of the arms of which will depend on the rate of movement. The time relations of the phases of the contraction can be obtained by placing beneath the lever a writing point attached to an electro-magnet thrown into action by a tuning-fork vibrating in hundredths of a second. In order to determine the rapidity with which the contraction follows the stimulation, it is essential that the moment of the latter be also recorded. This is accomplished by an automatic key, the opening or closing of which develops the stimulus which excites the muscle.

A combination of these different appliances constitutes a *myograph* and the curve of contraction a *myogram.* (See Fig. 23.)

It is necessary for the purpose of placing the excised muscle under mechanic conditions similar to those found in the body and for the registration of its movements under varying conditions to give the lever mass. This is accomplished by attaching weights to it beneath the muscle.

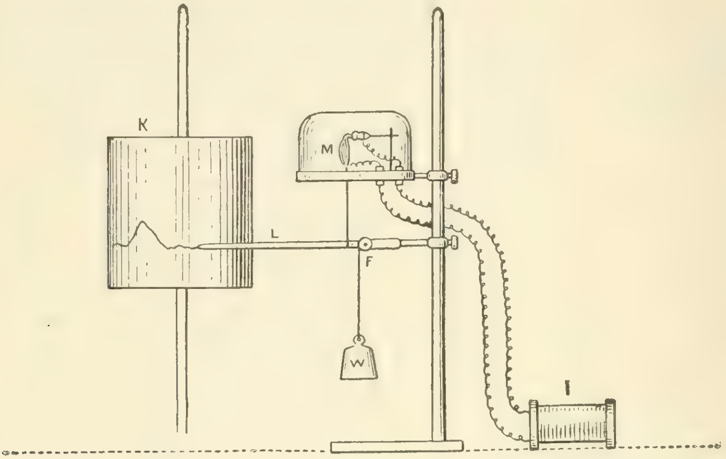

Fig. 23.—Myograph. K. Recording cylinder. M. Moist chamber. L. Recording lever. W. Weight. I. Induction coil.

The Isotonic Myogram.—With the object of obtaining a curve of the successive changes in the length of a muscle during a single contraction and at the same time avoiding changes in tension and therefore an acceleration of the lever, the weight attached to the lever should be applied close to its axis, in accordance with the isotonic method. The curve of contraction thus obtained is known as an isotonic myogram.[1]

With the muscle arranged as previously described and stimulated directly with a single induced electric current, the contraction will be recorded in the form of a curve similar to that represented in Fig. 24, in which the horizontal line represents the abscissa of time; a, the moment of stimulation; and b c d, the degree of shortening and the subsequent relaxation at each successive moment. The undulating line shows the time relations, the distance from crest to crest representing hundredths of a second. The curve may be divided into three portions:

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[1] The weighting of the lever or the loading of the muscle is accomplished in several ways: (1) The weight is attached to the lever just beneath or in the immediate neighborhood of the point of attachment of the muscle. This is known as the "loaded method" and has the effect of extending the muscle beyond its normal length previous to the moment of its stimulation and contraction. (2) The weight is attached to the lever at the same point as in the foregoing method, but by means of a support beneath the lever, the weight is prevented from extending the muscle previous to the moment of its stimulation and contraction. This is known as the "after-loaded" method. In either case a certain momentum is imparted to the weight, which continues after the muscle has ceased to act, both when shortening and relaxing, and so imparts to the recording lever additional movements which vitiate the true character of the curve. (3) The weight is attached to a small pulley on the axis of the lever and therefore at some distance from the point of attachment of the muscle. The advantage of this method lies in the fact that the initial tension of the muscle induced by the load remains practically constant throughout the contraction period and hence acceleration of the movement of the lever is prevented. This is known as the "isotonic method."

1. A short but measurable portion between the point of stimulation and the first evidence of the shortening, a b, known as the "latent period." The duration of this period for the skeletal muscle of the frog was originally determined to be 0.01 second, but with the employment of more accurate apparatus it has been reduced to 0.0025 to 0.004 second. During this period it is supposed that certain chemic changes are taking place preparatory to the exhibition of the movement. The duration of the latent period is influenced by a variety of conditions, *e.g.*, temperature, fatigue, strength of stimulus, etc.
2. An ascending portion, b c, the contraction or period of increasing energy. The contraction as shown by the character of the curve begins slowly, then proceeds rapidly, and again slowly as the shortening reaches its maximum. The contraction may be said to end when the tangent to the curve becomes parallel with the abscissa.

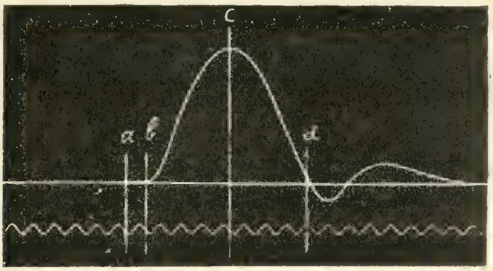


FIG. 24.—THE ISOTONIC MYOGRAM.

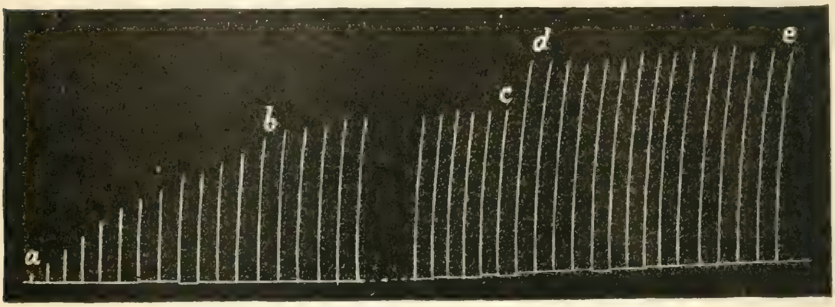
3. A descending portion, c d, the relaxation or period of decreasing energy. The relaxation as shown by the character of the curve begins slowly, then proceeds rapidly, and again slowly as the muscle attains its original length. The termination of the relaxation is at the point where the curve cuts the abscissa. The curve beyond this point may be complicated by the presence of one or more residual or after-vibrations, which are probably due to the inertia of the lever as well as to changes in the muscle elasticity.

The duration of the period of shortening is about 0.04 second, and of the period of relaxation 0.05 second. A single pulsation of the isolated muscle of the frog therefore occupies, from the moment of stimulation to termination, the tenth of a second. Muscles of many other animals have a contraction period the duration of which varies considerably from this. Thus, in man the time of a single contraction is one-twentieth of a second, in some insects one three-hundredth of a second, and in the turtle one second. Pale muscles have a shorter period than the red.

Influences Modifying the Effect of the Stimulus.—The contraction process in its entirety as well as in its individual parts is considerably modified by both external and internal conditions, among which may be mentioned the following:

1. *Character of the Stimulus.*—As the contraction is the response of the muscle to a stimulus, it may be inferred that the vigor of the former is proportional, within limits, to the strength of the latter. Thus using as a stimulus the single induced current, it has been found that if the

strength of the current is progressively increased, the height of the contraction will correspondingly increase until a certain maximum height is attained (Fig. 25, A, a b); then notwithstanding a continued increase in the strength of the stimulus, this height will not be exceeded for some time. But if the strength of the stimulus be yet further increased, there comes a moment when the contractions again increase in vigor and a second maximum height is attained (Fig. 25, B, d e). Beyond this no further increase in height is observed. The second maximum has been attributed to the presence in the muscle of two different substances differently affected by changes in temperature, by fatigue and by various drugs.



A. B.

Fig. 25.—Tracing Showing the Effects of a Gradual Increase in the Strength of the Stimulus on the Height of the Contraction. *a.* Minimal contraction; *a b.* progressive increase in the height; *b c.* first maximum (a number of contractions have been omitted for economy of space); *d e.* second maximum.

It has also been shown that the rate at which the muscle is stimulated with a given stimulus of uniform strength will influence the character of the contraction process. If the intervals between the successive stimulations be such as permit the muscle to recover from the effects of the contraction, it may contract as many as a thousand times without showing any particular variation from the normal form; but if the intervals are shorter than that just stated it is found that from the beginning of the stimulation each succeeding contraction slightly exceeds in height the preceding contraction, until a certain maximum is reached and maintained, indicating that for some reason the irritability and the energy of the contraction have been increased. This gradual increase in the height of the contraction has been termed the staircase effect, or the *treppe*. In the beginning of the period of stimulation there is sometimes observed a decrease in the height of the contraction following several stimulations before the staircase effect develops, indicating a temporary decrease in the irritability. These staircase contractions have been observed in the muscle of both warm-blooded and cold-blooded animals. The cause for this increase in irritability upon which the effect depends is attributed to the presence of certain chemic substances in the muscle arising as a result of its katabolism, such as carbon dioxid, mono-potassium phosphate, and paralactic acid. These compounds, when present in small amounts or in larger amounts for a short time, augment the action of the muscle and give rise to the treppe effect. (Lee.) In time, however, if the stimulation be continued, the irritability declines, the height of the contraction diminishes and finally the muscle ceases to respond to any stimulus.

2. *Variations in the Temperature.*—The temperature at which all phases of the contraction process, as represented by the myogram, attain their physiologic maximum value is about 30°C. If the temperature of the muscle falls to 20°C. there is a corresponding decline in activity, as shown by an increase of the latent period, a decrease in the height of curve—*i.e.*, in the shortening of the muscle—an increase both in the contraction and relaxation periods. As the temperature approaches 0°C, the height of the curve again suddenly increases, indicating, for some unknown reason, an increase in the irritability. This is, however, scarcely a physiologic condition. At a temperature of 40°C. to 50°C. the muscle suddenly contracts and passes into the condition of heat rigor or *rigor caloris.* The protein constituents of the muscle are coagulated and the irritability destroyed. (Fig. 26.)

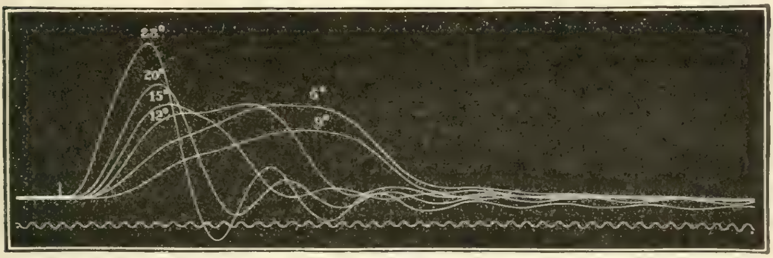


FIG. 26.—SINGLE CONTRACTIONS OF THE GASTROCNEMIUS MUSCLE AT DIFFERENT TEMPERATURES. Time tracing 200 per second.—(*Brodie.*)

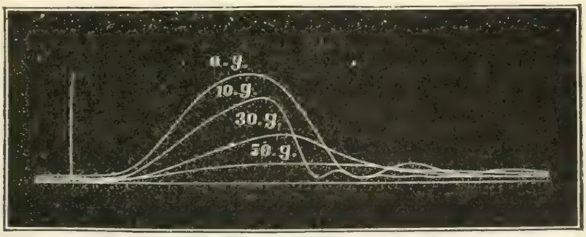


FIG. 27.—CONTRACTIONS OF A GASTROCNEMIUS MUSCLE WITH DIFFERENT LOADS.—(*Brodie.*)

3. *Variations in the Load.*—The extent to which a muscle is loaded or weighted will not only determine the height of the contraction, but also the time relations of all its phases. This is apparent from an examination of Fig. 27, in which it is shown that with an increase in load there is a decrease in the height of the contraction, an increase in the latent period, and a general increase in the duration of both the periods of rising and falling energy.

4. *Rapidly Repeated Stimulation.*—Prolonged or excessive activity of our own muscles is accompanied by a feeling of stiffness or soreness and lassi-

tude. There is at the same time a diminution in the speed and vigor of the contractions and the power of doing work. To this condition the term fatigue has been given. The cause of the fatigue is attributed to a diminution in the amount of the energy-yielding compounds as well as to the production and accumulation of waste products resulting from katabolic activity. Among the waste products, mono-potassium phosphate, paralactic acid, and carbon dioxid are the most important. These substances, when present in small amounts or in larger amounts for a short time, increase the irritability of the muscle, but when they accumulate more rapidly than they are removed, as is the case during excessive activity, they exert a depressive influence on the irritability of the muscle and thus diminish its contractile power and its capacity for doing work. The more rapidly they are removed, the sooner is a fatigued muscle restored to its normal condition. The condition of fatigue with its attendant phenomena is shown by stimulating through its nerve an excised frog muscle with induced electric currents at intervals of one second. In a variable period of time the muscle shows an increase in the duration of the latent period, a diminution of the height of the contraction, in the power of doing work, and an increase in the time required for relaxation. (Fig. 28.) If the stimulation is continued the contractions gradually decline as the muscle becomes exhausted. When a muscle will no longer respond to stimulation through its related nerve, it can be made to respond to direct stimulation with the electric current. This taken in connection with the fact that stimulation of a nerve-trunk even for several hours does not fatigue it, leads to the inference that the cause of the cessation of contraction does not lie wholly in the muscle but partly in the nerve endings in the muscle. These structures it is believed fatigue more readily than the muscle structures, and hence fail to conduct the nerve impulse to the muscle. By this means it is protected from absolute exhaustion.

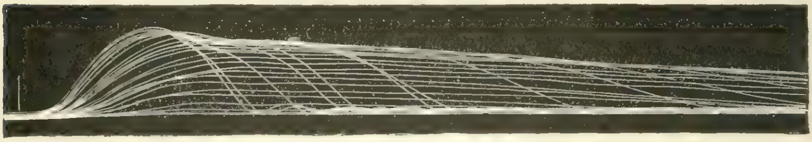


FIG. 28.—FATIGUE CURVES. EVERY TWENTIETH CONTRACTION RECORDED.

5. *Nutrition.*—The irritability of a muscle which conditions the contraction process is dependent on the maintenance of its nutrition; hence a continuous and sufficient supply of nutritive material and a rapid removal of waste products are essential conditions for the exhibition of normal contractions. A diminution of blood supply or an accumulation of waste products sooner or later impairs the irritability and diminishes the vigor and extent of the contraction. Various drugs—*e.g.*, veratrin, barium, etc.—introduced into the circulation and finding their way into the muscle modify the contraction process, as shown by a very great increase in the duration of the relaxation period.

The Isometric Myogram.—With the object of obtaining a curve of the increase and decrease in the tension of a muscle during a single contraction, with the exclusion as far as possible of a change in length, the muscle may be made to contract against a strong spring or similar resistance practically though not absolutely sufficient to prevent shortening. To this method the term isometric has been given, and the curve so obtained is an *isometric myogram* or a *tonogram*. The recording portion of the lever is prolonged some distance so that the very slight upward movement at its axis, close to which the muscle is attached, will be considerably magnified. That the ordinate value of an isometric curve may be known, the apparatus must be graduated by subjecting the spring to a series of weights playing over a pulley supported by the muscle clamp.

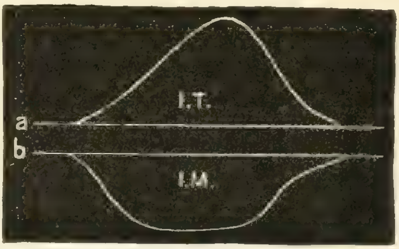


Fig. 29.—a. Diagram of Isotonic; b, of Isometric Muscle Curves.—(*Landois and Stirling.*)

The curve of the variation in tension obtained by the isometric method is shown in Fig. 29, b, in which the two curves are contrasted. The form of the curve indicates that the muscle attains its maximum of tension more rapidly than its maximum of shortening; that the tension endures for a certain period of time unchanged; that the fall in tension takes place more rapidly than the muscle lengthens.

The Myogram Due to the Make and the Break of a Galvanic Current.—The contraction of the muscle which has heretofore been recorded has been caused by the momentary action of an induced current. The contraction of the muscle which is caused by the action of a constant or galvanic current presents features which are somewhat different and, as it serves to illustrate the difference in the effects of a constant or galvanic and an induced or interrupted current, a myogram of a contraction due to the make and break of a galvanic current is introduced at this place. The effects which are observed in a muscle during the passage of both feeble and strong currents have been alluded to in a previous section. (See page 57.) In Fig. 30 these effects are graphically represented. It will be observed that on the closure of the circuit at c the muscle at once contracted and so long as the current was flowing, the muscle remained in a more or less contracted state known as galvanotonus; on opening the circuit at o the muscle again con-

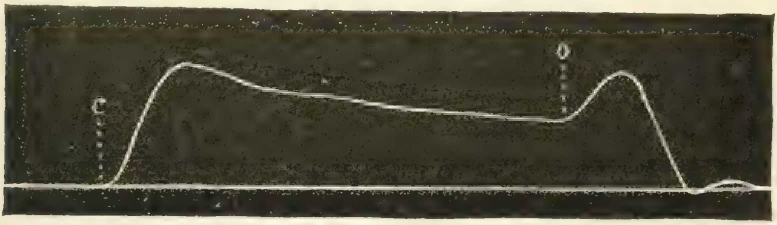


Fig. 30.—Myogram Due to the Action of a Galvanic Current, Applied Directly to a Muscle, when the Circuit was Closed (*c*) and when it was Opened (*o*).

tracted, after which it gradually relaxed and returned to its original condition. The record shows also that during the actual passage of the current the muscle substance was being stimulated by it.

The Work Accomplished by a Muscle during the Time of a Single Contraction.—By work is meant the overcoming of opposing forces. In the physiologic activities of the body the muscles at each contraction not only overcome the resistances of antagonistic muscles, the weight of the limbs, the friction of joints, etc., but in addition overcome various external resistances connected with the environment—*e.g.*, gravity, cohesion, friction, elasticity, etc. The muscles may therefore be regarded as machines for the accomplishment of work. Experimentally the work done by an isolated muscle may be calculated if the height of the contraction is first obtained and then multiplied by the weight raised. The influence of the weight on the height of the contraction is shown in Fig. 31, in which only the height of the contraction or the degree of shortening and hence the lift of the weight is represented. From this tracing it will be observed that the extent to which a muscle will shorten in response to a maximal stimulus is greatest when it is unweighted; but as weights differing by a common increment are added, the height of the contraction diminishes until with a given weight it is *nil*.

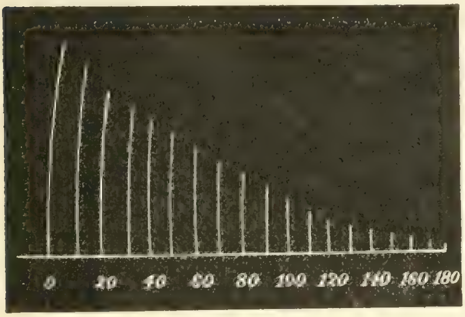


Fig. 31.—Tracing Showing the Gradual Diminution in the Height of the Contraction as the Weight was Increased by a Common Increment of 10 Grams from 0 to 180 Grams. Magnification of the Lever, 4.

A careful study of the results of this experiment will show that the work done gradually increased as the load was increased from 0 to 70 grams, when it amounted to 210 gram-millimeters; but that after this, even though the weight lifted was greater, the height to which it was lifted was less, and hence the work done gradually decreased, until it amounted to nothing.

The following table will also show the work done by a frog's muscle according to Rosenthal.

Weight.	Height.	Work Done.
0 grams	14 mm.	0 gram-millimeters.
50 grams	9 mm.	450 gram-millimeters.
100 grams	7 mm.	700 gram-millimeters.
150 grams	5 mm.	750 gram-millimeters.
200 grams	2 mm.	400 gram-millimeters.
250 grams	0 mm.	0 gram-millimeters.

From the preceding figures it is evident that the mechanical work of a muscle increases with increasing weights up to a certain maximum, and then declines to zero. Equally when the muscle contracts to its maximum without being weighted, and when it does not contract at all from being overweighted, no work is done. Between these two extremes the muscle performs varying amounts of work.

Absolute Muscle Force.—The maximum amount of force which a muscle puts forth during a contraction is naturally measured by the amount of work done; but as this varies with the degree to which the muscle is weighted, another measure has been adopted, to which the term absolute muscle force or static force has been given. The absolute force is measured by the weight which a muscle can raise and hold at its natural length after it has been extended by this weight. In Fig. 22 this weight would be on the abscissa B b′ where it is cut by the extension curve of the active contracted muscle. The absolute force is also measured by the weight which is just sufficient to prevent the muscle from shortening when stimulated. This is best determined by the method of after-loading in which the muscle is not extended by the weight previous to the contraction. It has been found that the absolute force of a muscle is directly dependent on the number and not the length of the fibers it contains and proportional to the physiologic transverse section of the muscle. The transverse section of a muscle is obtained by dividing its volume (obtained by dividing its actual weight by the specific weight of muscle-tissue, 1.058) by the average length of the fibers. Assuming that the muscle weighs 609 grams, its volume would be 576 c.c.; and if it be further assumed that the fibers have an average length of 4 centimeters the transverse section would contain 114 sq. centimeters each of which would have a length of 4 centimeters.

For purposes of comparison it is customary to refer the absolute force to the units of area—viz., one square centimeter. Rosenthal estimates the force for the square centimeter of the muscle of the frog at from 2 to 8 kilograms; for the muscles of man at 6 to 8 kilograms; Koster at about 10 kilograms for the muscles of the leg and 7 to 8 kilograms for the muscles of the arm.

Summation Effects.—If a series of successive stimuli be applied to a muscle, the effect will vary according to the rapidity with which they follow one another. As previously stated, if the interval preceding each stimulus be sufficiently long to enable the muscle to recover from the effects of the previous contraction, there will be no change in the form or the character of the contraction for a long time except a slight increase, in the early period, of the irritability as shown by the increased height of the curve or shortening of the muscle. If, however, a second stimulus be applied to a muscle during the period of relaxation, a second contraction immediately follows which is added to or superposed on the first; the effect produced will be greater than that produced by either stimulus separately. (See Fig. 32.)

A third stimulus applied during the relaxation of the second contraction produces a third contraction which adds itself to the second, and so on. The increment of increase in the extent of the successive contractions gradually diminishes, however, until the muscle reaches a maximum of contraction. The superposition of the second contraction on the first, the third on the second, and so on, is termed *summation of contractions or effects.* Experiment has shown that the greatest effect of a second stimulus—that is, the highest contraction—is produced when the stimulus is applied during the last third of the period of rising energy, when the sum of the two contractions is almost twice as great as the first contraction would have been. (Fig. 32.) The effects following both maximal and submaximal stimuli indicate that the muscle cannot attain its maximum of shortening except through a summation of several stimuli. If a second maximal stimulus enters a muscle during the latent period following the first, the effect produced will be no greater than that produced by a single stimulus. The muscle during this period is said to be refractory or non-responsive to a second stimulus. If, however, the stimuli are submaximal they add themselves together, and though the effect is but a single contraction, it is larger than either would have produced separately. This is termed the *summation of stimuli.*

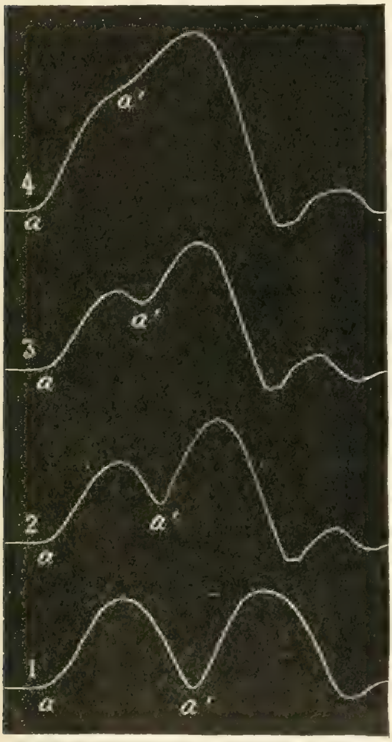


Fig. 32.—Tracing Showing the Effects of Two Successive Stimuli, *a. a'* with Gradually Diminishing Interval on a Muscle Contraction. To be read from below upward.

Still further, if a series of subminimal stimuli, each of which is alone insufficient to produce a contraction of the muscle, be applied in rapid succession, a contraction frequently results. This is termed the *summation of subminimal stimuli.*

Tetanus.—Tetanus may be defined as a more or less continuous contraction of a muscle which arises when the time intervals between the stimuli are shorter than the time of the contraction process. Tetanus will be incomplete or complete according to the number of stimuli that reach the muscle in a second of time. When a muscle is stimulated directly or, better, indirectly through its related nerve by a series of induced currents at the rate of four or six per second, it undergoes a corresponding number of contractions of about equal extent. If the rate of stimulation is increased up to the point when the interval between each stimulus is less than the duration of the entire contraction process, the muscle does not have time to relax completely before the arrival of the succeeding stimulus, and hence remains in a more or less contracted state, during which it exhibits a series of alternate partial contractions and relaxations. To this condition of muscle activity the term incomplete tetanus or clonus is applied. A graphic record of an incomplete tetanus is given in Fig. 33.

In such a tracing it is observed that the second stimulation, occurring before the muscle had time to relax, gave rise to a second contraction, which was superposed on the first; the same result followed the third stimulus, the fourth, the fifth, and so on. Owing largely to this summation of the contractions there is a gradual rise in the height of the contraction curve. This condition of the muscle, viz., continued contraction, combined with diminished power of relaxation, is termed *contracture.* The tracing also shows that as the stimulus continues, the base line, that connecting the lowest points of the contractions, gradually rises and takes the form of a curve which increases in height as the stimulus continues. The apex line, that connecting the highest points of the contractions, also rises at the same time, indicating a continuous increase in the height of the contractions. The length of time a muscle will exhibit incomplete tetanus depends on a variety of circumstances, *e.g.*, character of muscle, rate and strength of stimulation, etc., but mainly on the rapidity with which the muscle becomes fatigued. With the oncoming of fatigue the muscle begins to relax, and ultimately returns to its normal condition, notwithstanding the continued stimulation. If the stimulation be withdrawn, the muscle does not at once return to its original length but remains more or less contracted for a variable time. This contraction after stimulation is known as the contraction-remainder.

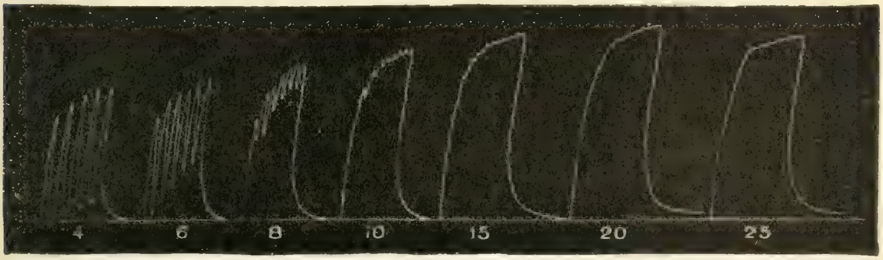


FIG. 33.—CURVES SHOWING THE ANALYSIS OF TETANUS OF A FROG'S MUSCLE (GASTROCNEMIUS). The numbers under the curves indicate the number of shocks per second applied to the muscle. There is almost complete tetanus with twenty-five per second, and it is a little lower than the previous one because the muscle was slightly fatigued.—(*Stirling.*)

If the stimulation be still further increased in frequency, the individual contractions become fused together and the curve described by the lever becomes a continuous line. (See Fig. 33.) Notwithstanding the fact that the individual contractions are no longer visible, it can be shown by other methods that the muscle is undergoing a series of slight alternate contractions and relaxations or vibrations at least. After a varying length of time the muscle becomes fatigued, relaxes, and returns to its natural condition even though the stimulation be continued. The number of stimuli per second necessary to develop complete tetanus will depend under normal circumstances on the period of duration of the individual contractions. The longer this period, the less the number of stimuli required, and the

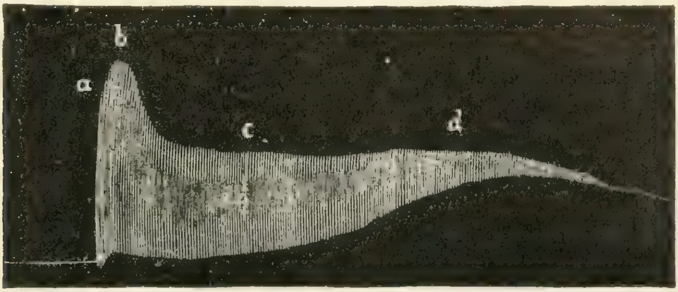


FIG. 34.—DEVELOPMENT OF FATIGUE AND CONTRACTION. Muscle stimulated once a second by a strong induced current.

reverse. Hence the number of stimuli will vary for different classes of animals and for different muscles in the same animal, *e.g.*, 2 or 3 for the muscles of the tortoise, 10 for the muscles of the rabbit, 15 to 20 for the frog, 70 to 80 for birds, 330 to 340 for insects.

An effect which follows frequent stimulation of a muscle, *e.g.*, 50 to 60 times per minute, and especially when the muscle is somewhat fatigued or cold is shown in Fig. 34. It is evidently a combination of contracture and fatigue. It will be observed that at the beginning of the stimulation there is a staircase effect, a–b, combined with diminished relaxation. This in turn is followed by a decline in the height of the contractions, b–c, and a fall of the base line which may be attributed to fatigue conditions. After a short time there is a second rise of the base line, d, and a rapid development of contracture. The muscle at this period is in a condition of incomplete tetanus which gradually passes into complete tetanus attended by fatigue.

The tetani of muscles may be classified in accordance with their causes as follows:—

1. Physiologic
    - Volitional.
    - Reflex.
2. Experimental.
3. Pharmacologic.
4. Pathologic
    - Bacterial.
    - Reflex.

1. Physiologic Tetanus. 1. *Volitional.*—Because of the fact that during the continuance of a volitional movement the muscle is in a state of continuous contraction, it may be accepted that volitional contractions are states of tetanus, more or less complete; for the shortest possible volitional contraction, however quickly it takes place, has always a longer duration than a single contraction caused by an induced electric current. As the volitional contraction is similar to that observed when a muscle or its related nerve is stimulated by rapidly repeated induced currents, it is assumed that the nerve-cells in the spinal cord are discharging in a rhythmic manner a certain number of nerve impulses per second in consequence of the arrival of nerve impulses coming from the cerebral cortex, the result of volitional acts. In other words the volitional tetanus is the result of a discontinuous stimulation. The number of stimuli transmitted to a muscle during a volitional tetanus has been estimated by the employment of the graphic method at from 8 to 13 per second, 10 being about the average. When a volitional contraction is recorded the myogram not infrequently exhibits a series of small wave-like elevations which indicate that the muscle is not in a state of complete tetanus but is undergoing slight alternate contractions and relaxations. Unless the contraction process in human muscle differs from that of frogs it is difficult to see how 10 or even 20 stimuli per second can give rise to even an incomplete tetanus when the single contraction is $\frac{1}{20}$ of a second in duration.

2. *Reflex.*—A tetanus of muscle, physiologic in character, arises during the performance of many muscle movements in consequence of peripherally acting causes and may therefore be termed a reflex tetanus. The duration of a tetanus thus induced, like the duration of a volitional tetanus, will vary

with the duration of the exciting cause. Reflex tetani are presented by the muscles of the lower jaw during mastication, by the intercostal muscles during breathing, by the muscles of the limbs during walking, etc. In these and other instances there are reasons for believing that for a variable period of time the muscles are in a state of continuous contraction from the discharge of nerve impulses from the nerve cells in the spinal cord as the result of the arrival of nerve impulses coming from a peripheral surface.

2. **Experimental Tetanus.**—The tetanus of muscle developed in accordance with the method described in foregoing paragraphs, *i.e.*, by the employment of instrumental procedures, may be termed experimental tetanus. Its mode of development serves to illustrate and explain the method by which individual contractions are summated and continuous contractions made possible for the performance of volitional acts.

3. **Pharmacologic Tetanus.**—The administration of certain drugs, *e.g.*, strychnin, in sufficient amounts, is followed in a short time by a series of intermittent spasms in which all the muscles of the body are involved. At the beginning of the spasms the muscles are thrown into tonic or complete tetanus, during the continuance of which the muscles are hard and firm. In a short time this tonic state begins to subside, giving way to tremors or a series of irregular contractions resembling incomplete tetanus or clonus. A tetanus of this character may be termed pharmacologic. Though the onset of the tetanus is occasioned largely by peripheral stimulation, the seat of action of strychnin is central and for the most part focalized in the spinal cord. The exact seat of its action is not definitely determined but there are reasons for believing that it is on the end-tufts of afferent nerves in the spinal cord or on the intercalated neuron between them and the nerve-cells in the anterior horns of the gray matter, the irritability of which is raised and the resistance to the transmission of nerve impulses coming from the periphery diminished. As a result the nerve impulses are transmitted to the nerve-cells more readily, not only in a horizontal but also in a longitudinal direction, and the effects they produce enormously increased.

4. **Pathologic Tetanus.** 1. *Bacterial.*—The introduction of a specific bacillus into a wound in any region of the body is followed after a period of incubation of from three or four days to a week by a tetanus in which nearly all the muscles of the body are involved, characterized by a tonic contraction and clonic exacerbations. A tetanus of this character may be termed pathologic. The persistent tonic contraction is the result of a more or less continuous discharge of nerve impulses from the nerve-cells of the spinal cord which have been rendered abnormally irritable by the action of a toxin, produced by the bacilli, and having a selective action on these structures. The clonic exacerbations are evoked from time to time by various forms of peripheral stimulation.

2. *Reflex.*—A tetanus of individual muscles more or less continuous in character is occasionally the result of peripheral irritations of a pathologic character. A tonic contraction of the masseter muscles, for example, firmly closing the jaws for weeks and months at a time is caused in some instances by an impacted wisdom tooth or an ulcerative condition of the mouth. Since the removal of the cause is followed by a relaxation of the muscle, this form of tetanus, known as *trismus*, may be regarded as pathologic in character and reflex in origin.

The Muscle Sound.—If a stethoscope or a myophone with telephone connections be placed on a muscle while in a condition of volitional tetanus and at the same time kept in a certain degree of tension, there will be developed in the observer a sensation of sound or tone which is spoken of as a muscle sound or tone. It is also readily heard in the masseter muscle when the side of the face is placed on a receiving body such as a pillow, and the masseter muscles made to contract volitionally. This tone is attributed to a vibration or an alternate contraction or relaxation of the muscle or to an intermittent rhythmic variation in tension, the result of the rate of stimulation. This tone corresponds to a vibration frequency of from 18 to 20 per second and is accepted as one of the proofs that the physiologic volitional tetanus is not continuous but discontinuous in character. If a muscle is tetanized with induced currents, the tone increases in pitch for a limited time as the frequency of the current per second increases up to a certain maximum, which for frogs is about 200 and for mammals about 1000.

CHEMIC PHENOMENA

The chemic changes which underlie the transformation of energy in the living muscle even when in a state of relative rest are active and complex, though but little is known as to their exact character. As shown by an analysis of the blood flowing to and from the resting muscle, it has, while flowing through the capillaries, lost oxygen and gained carbon dioxid. The amount of oxygen absorbed by the muscle (9 per cent.) is greater than the amount of carbon dioxid (6.7 per cent.) given off. Notwithstanding the relation of the oxygen absorbed to the carbon dioxid produced, there is no parallelism between these two processes, as the carbon dioxid will be given off in the absence of free oxygen or in an atmosphere of nitrogen.

If the muscle be stimulated through its related nerve all the chemic changes are increased as shown both by an increased absorption of oxygen and an increased production of carbon dioxid, though the ratio existing between them differs considerably from that of the resting muscle. Thus, according to Ludwig, an active muscle absorbs 12.26 per cent. of oxygen and gives off 10.8 per cent. carbon dioxid. At the same time the muscle-tissue changes from a neutral to an acid reaction, from the development of sarcolactic acid and possibly phosphoric acid. The degree of the acidity depends partly on the duration of the contraction periods. Chemic analysis of a tetanized muscle shows that it contains less glycogen than a resting muscle, and that it contains a larger amount of water. Coincident with the muscle contraction, the blood-vessels become widely dilated, leading to a large increase in the blood-supply and a rapid removal of the products of decomposition.

Rigor Mortis.—A short time after death the muscles pass into a condition of extreme rigidity or contraction known as death stiffening or *rigor mortis*, which lasts from one to five days. In this state they offer great resistance to extension. At the same time their tonicity disappears, their cohesion diminishes, and their irritability ceases. The time of the appearance of this post-mortem rigidity varies from a quarter of an hour to seven hours. Its onset and duration are influenced by the condition of the muscle irritability at the time of death. When the irritability is impaired from any cause, such as chronic disease or defective blood-supply, the rigidity appears promptly but is of short duration. After death from acute diseases it is apt to be delayed, but will continue for a longer period. The rigidity first appears in the muscles of the lower jaw and neck; next in the muscles of the abdomen and upper extremities; finally in the trunk and lower extremities. It disappears in practically the same order. Chemic changes of a marked character accompany this process. The muscle becomes acid in reaction from the development of sarcolactic acid and there is a large increase in the amount of carbon dioxid given off. The immediate cause of the rigidity appears to be coagulation of the myosin and myogen within the sarcolemma with the formation of two insoluble proteins, myosin fibrin and myogen fibrin. In the early stages of the coagulation restitution is possible by the circulation of arterial blood through the vessels. The final disappearance of this post-mortem rigidity is due probably to the action of acids which render the myosin and myogen fibrins soluble, and possibly to the action of various microörganisms which give rise to putrefactive changes.

Source of the Muscle Energy.—The nature of the materials which are the immediate sources of the muscle energy has been the subject of much discussion. The absence of any noticeable increase in the quantity of urea or other nitrogen-holding compounds excreted renders it probable that the energy does not come from the metabolism of protein materials. The marked production of carbon dioxid and sarcolactic acid points to the decomposition of some unstable compound, of a carbohydrate character, rich in carbon and oxygen. As the result of many investigations it has come to be believed that glycogen is the compound which furnishes the energy under physiologic conditions, inasmuch as this substance, generally present in muscle, disappears during activity. A muscle which has been tetanized contains less glycogen than the corresponding muscle at rest. A muscle which has been separated from the nervous system by division of its nerves and thus prevented from contracting accumulates glycogen. Bunge is of the opinion that though the carbohydrates are the main, they are not the only sources of muscle energy. If there is a deficiency or absence of carbohydrate food, the muscle will utilize fat and protein, for experiment has shown that the available glycogen is entirely consumed by the second or third day. The mechanism by which the energy is liberated, whether by direct oxidation or decomposition is uncertain. The general trend of experimental investigation points to the disruption of some carbohydrate, perhaps glucose, derived from the stored glycogen and the oxidation of the intermediate products to carbon dioxid and water. The oxidizable compound appears to be lactic acid. For if the muscle be made to contract in an atmosphere deficient in oxygen, the amount of lactic acid produced is relatively large and the amount of carbon dioxid relatively small. If the surrounding atmosphere be rich in oxygen, the reverse conditions obtain. Under physiological conditions, when the muscle is supplied with blood containing its customary percentage of oxygen it is probable that the products set free by the disruption of the sugar molecule are rapidly oxidized to CO_2 and H_2O, with the liberation of their contained energy. But the fact that muscle will contract in an atmosphere free of oxygen, that no free oxygen can be obtained from muscle, would support the idea that the mechanism is one of decomposition. Hermann suggests that the energy of a contraction is liberated by the splitting and subsequent re-formation of a complex body belonging neither to the carbohydrates nor fats, but to the proteins—to this hypothetic body the term inogen is given. This complex molecule, the product of the nutritive activity of the muscle-cell in undergoing decomposition, would yield carbon dioxid, sarcolactic acid, and a protein residue resembling myosin. On the cessation of the contraction the muscle-cell recombines the protein residue with oxygen, carbohydrates, and fats, and again forms the energy-holding compound, inogen. The phenomena of rigor mortis support this view. At the moment of this contraction the muscle gives off CO_2 in large amount, develops sarcolactic acid and myosin. There is thus a close analogy between the two processes; in other words, a contraction is a partial death of the muscle. If this view is correct, then the oxygen is required mainly for heat production through oxidation processes.

THERMIC PHENOMENA

The potential energy liberated in a muscle on the arrival and subsequent action of a nerve impulse, manifests itself partly as heat and partly as mechanic motion or a change of shape of the muscle. Though heat production is taking place even during the passive condition, it is largely increased by muscle activity. The amount of heat produced will vary however with a variety of conditions, as strength of stimulus, tension, work done, etc.

Stimulus.—It has been experimentally determined that the skeletal muscle of the frog, the gastrocnemius, shows after a single contraction a rise in temperature of from 0.001°C. to 0.005°C. and after tetanization an increase of from 0.14°C. to 0.18°C. It has also been shown that an increase in the strength of the stimulus from a minimal to a maximal value increases the amount of heat liberated. This is the direct result of increased chemic change naturally following increased stimulation.

Tension.—The greater the tension of a muscle, the greater, other conditions being the same, is the amount of heat liberated. If the muscle is securely fastened at both extremities so that shortening is practically impossible during the stimulation, the maximum of heat production is reached. In the tetanic state the great increase in temperature is due to the tension of antagonistic and strongly contracted muscles. In both instances, mechanic motion being prevented, the liberated energy is transformed into heat.

Mechanic Work.—If the muscle is permitted to shorten and raise a weight, some of the energy liberated takes the form of mechanic motion. If the weight is removed at the height of the contraction, external work is accomplished. The greater the weight raised, within limits, the greater is the percentage of energy which takes the direction of mechanic motion. The percentage of the total energy liberated which is thus utilized, has been estimated at from 25 to 40 per cent. In accordance with the law of the conservation of energy, the heat produced, stated in calories, plus the energy required in the raising of the weight, expressed in kilogrammeters of work, must equal the potential energy transformed.

A muscle during a tetanic contraction of short duration accomplishes more work than during a single contraction, the weight in each case being the same. In the former condition the height of contraction through summation, and hence the work done, is greater than in the latter. The work done by a short tetanic contraction may be two or three times that of a single contraction, but after the muscle reaches its maximum degree of shortening and then continues in a state of tetanus, no further work is done. Internal work is done, however, *i.e.*, the continuous liberation of energy, as shown by an increase in the temperature.

When a weight which is lifted by a muscle during a single contraction is allowed to act on the muscle during the relaxation, no external work is accomplished. All the energy set free manifests itself as heat. Internal work is done, as shown by the fact that the muscle becomes fatigued.

Work Done Daily.—The muscle system in its entirety is to be regarded as a machine for the transformation of potential into kinetic energy, and in so doing accomplishes work. Through the intermediations of the bones of the skeleton which play the part of levers the individual not only changes his position in space, but overcomes to some extent the resistances offered by the environment. The employment of artificial levers, tools, as distinguished from natural levers, bones, materially adds to the effectiveness of the muscle machine. The amount of work which a man of average physical development weighing 72 kilos can perform in eight hours has been variously estimated. It will naturally vary according to the character of the occupation. If the work done be calculated from the number of kilograms raised one meter, the average laboring-man performs about 300,000 kilogrammeters of work.

ELECTRIC PHENOMENA

Electric Currents from Injured Muscles.—The energy liberated as the result of the action of a nerve impulse is not only transformed into heat and mechanic motion, but to some extent also into electric energy. The presence of points of different potential on the surface of the muscle, the necessary condition for the development of electric currents, is tested by means of non-polarizable electrodes connected by wires with a sensitive galvanometer or capillary electrometer. When such electrodes are brought in contact with a muscle properly prepared, there is at once developed and conducted to the galvanometer an electric current the intensity and direction of which are indicated by the deflection of the galvanometer needle. The existence of this current is most conveniently demonstrated with single muscles the fibers of which are parallel—*e.g.*, the sartorius, or the semimembranosus of the frog. If the tendinous ends of either of these muscles be removed by a section made at right angles to the long axis, a muscle prism is obtained which presents a natural longitudinal surface and two artificial transverse surfaces. A line drawn around the surface of such a muscle prism at a point midway between the two transverse sections constitutes the equator.

When the natural longitudinal and artificial transverse surfaces are connected with the wires of a galvanometer the terminals of which are provided with non-polarizable electrodes, an electric current is at once developed. In all instances the current, as shown by the deflection of the needle, originates at the transverse surface, passes through the muscle to the longitudinal surface, thence through the galvanometer to the transverse surface. The longitudinal surface is, therefore, electropositive, the transverse surface electronegative. The two points exhibiting the greatest difference of potential, and hence the most powerful current, lie in the equator and in the center of the transverse surface. Currents of gradually diminishing intensity are obtained when the electrode placed on the longitudinal surface is removed toward either end. Feeble currents are developed when two points situated at unequal distances, either on corresponding or opposite sides of the equator, are connected; in either case the current flows from the point lying nearest the equator to the point farthest from it. Similar currents are obtained when two points on the cross-section situated at unequal distances from the central axis are connected, in which case the direction of the currents will be from the point lying nearest the periphery toward the center. On the contrary, no current is developed when two points on the longitudinal surface equally distant from the equator, or two points on the transverse surface equally distant from the central axis, are connected. Such points are said to be isoelectric. These facts are shown in Fig. 35. The natural ends of the muscle, enclosed by sarcolemma and tendon, do not exhibit, if carefully preserved from injury, the negativity characteristic of the artificial transverse ends.

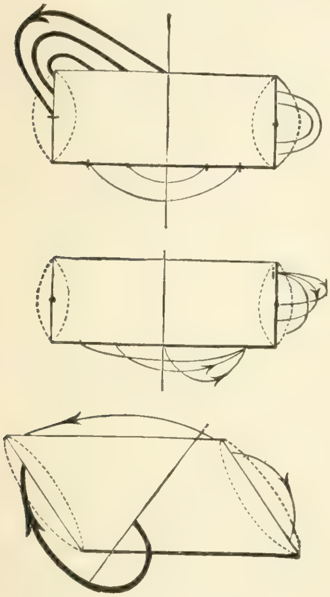


FIG. 35.—DIAGRAM TO ILLUSTRATE THE CURRENT IN MUSCLE. The arrowheads indicate the direction; the thickness of the lines indicates the strength of the currents. —(*Landois and Stirling.*)

Similar electric conditions are exhibited by the muscles of man and other mammals, by the muscles of birds, reptiles, amphibia, etc. The currents developed by connecting the equator on the longitudinal surface with the axis of the transverse surface have an electromotive force in the frog muscle of from 0.037 to 0.075 of a Daniell cell.

The electric currents in the muscle are intimately associated with the chemic changes underlying its nutrition, and hence their intensity rises and falls with all the conditions which maintain or impair muscle nutrition and irritability. The currents observed in the injured muscle during the inactive state have been termed *currents of rest.* Du Bois-Reymond regarded them as pre-existent, intimately connected with the living condition of the muscle, and essential to the performance of its functions, and to be explained by the view that the entire muscle is composed of molecules each of which exhibits the same difference of potential on its longitudinal and transverse surfaces as the muscle prism itself. Hermann denies the existence of currents in normal resting muscle and attributes them to injuries of the surface, due to methods of preparation, in consequence of which the tissue dies and becomes electronegative to the uninjured area, which remains electropositive. These currents Hermann terms "demarcation currents."

Negative Variation of the Muscle Current.—If a muscle exhibiting a current of injury be excited to activity by tetanizing induced currents applied to the opposite end of the muscle, it will be observed that as the contraction wave passes over the muscle there is a movement of the galvanometer needle toward the zero point, indicating a diminution of the potential on the longitudinal surface. To this diminution in the strength of the current the term *negative variation* was given. On the withdrawal of the stimulus the needle again returns in a short time to its former position. The diminution of potential on the longitudinal surface of the muscle is now attributed to the passage of the excitation and contraction processes, to a temporary disintegration of the muscle substance (Fig. 36). With their disappearance and the subsequent restoration of the nutrition of the muscle, the former electric condition returns.

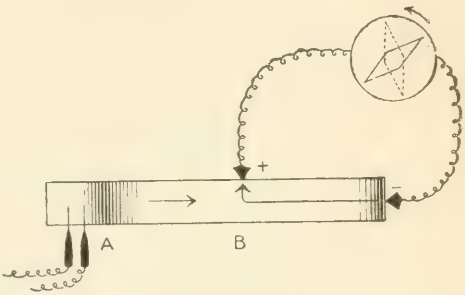


Fig. 36.—The Negative Variation of the Demarcation Current. A. The contraction wave, which as it passes beneath the electrode at B causes a diminution of potential.

The primary deflection of the galvanometer needle is due to the demarcation current which arises as a result of the difference in electric potential produced by the destructive chemic changes taking place at the cut end of the muscle. The negative variation is caused by the fact that the activity of the muscle, with its attendant chemic changes, will always be greater in the uninjured equatorial region, and hence will always tend to counterbalance the original source of difference in electric potential.

Electric Currents from Non-injured Muscles.—Though perfectly normal resting muscle, according to Hermann, is isoelectric, nevertheless electric currents are developed during activity to which he has given the term action currents, and which are attributed to the propagation of the contraction wave.

Action Currents.—When two isoelectric points on the longitudinal surface of a muscle are connected with a galvanometer and a single stimulus applied directly to one extremity, it can be shown that as the contraction wave passes beneath A, Fig. 37, the muscle-tissue at that point becomes electronegative toward B and a current at once passes through the galvanometer from B to A, as shown by the deflection of the needle toward A. As the contraction wave passes beneath B it in turn becomes electronegative, and a temporary condition of equal potential is established when the needle returns to the zero point. In a very short time the nutrition of A is restored and becomes electropositive toward B, when a current will pass through the galvanometer in the opposite direction from A to B, as shown by the movement of the needle toward B, Fig. 38. As the contraction wave passes beyond B its nutrition is restored and becomes of equal potential with A. The term phasic is applied to these currents. The first current flows in the muscle in the direction of progress of the contraction wave—first phase; the second current flows in the reverse direction—second phase; the current is therefore diphasic. When a muscle is tetanized, there is but a single current observed, which, however, endures so long as the tetanic contraction is maintained. To this current the term decremential is given. When a muscle is excited to action by the nerve impulse which enters at its center, two contraction waves are developed, one in each half of the muscle, and hence there are two sets of diphasic action currents.

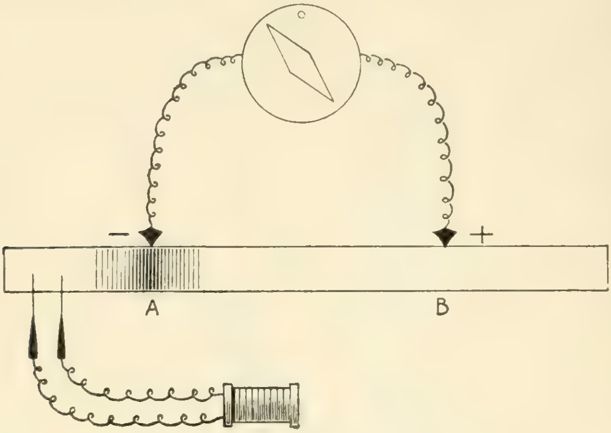


Fig. 37.—The Condition Leading to the Development of the First Action Current.

The presence of action currents in the muscle of the living body during a single contraction was demonstrated by Hermann in the muscles of the forearm. The arrangement of the experiment was, briefly, as follows: The forearm was surrounded by two twine electrodes saturated with zinc solution, one being placed at the physiologic middle—the nervous equator—the other at the wrist. Both electrodes were then connected with the galvanometer. When the brachial plexus was stimulated in the axillary space, the deflections of the galvanometer needle, when analyzed with the repeating rheotome, indicated phasic currents with a single contraction. In the first

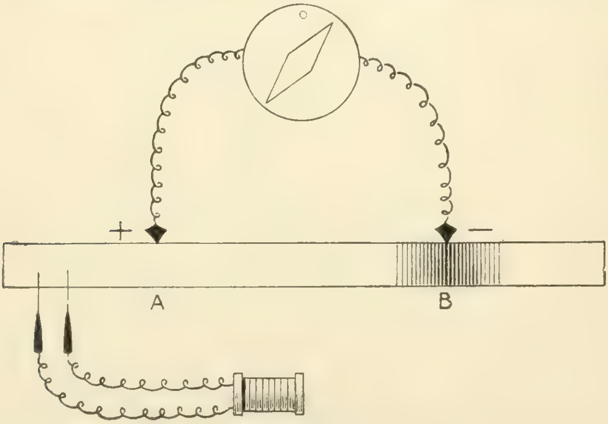


Fig. 38.—The Condition Leading to the Development of the Second Action Current.

phase—atterminal—the wrist became positive and the current passed in the muscle toward its termination; and in the second—abterminal—it became negative and the current now passed in the reverse direction. The action currents which are observed in the frog's muscle were thus shown to be present in the living human muscle, with this difference, however: that the second phase—abterminal—instead of being weaker in man, is equally strong with the atterminal. This experiment also revealed the fact that the rapidity of propagation of the excitation wave was much greater in man, amounting to about twelve meters per second. Hermann therefore denies the pre-existence of electric currents and regards them as due to localized temporary disintegration of the muscle in consequence of activity, as they disappear on the restoration of the muscle to its normal condition.

SPECIAL ACTION OF MUSCLE GROUPS

The individual muscles of the axial and appendicular portions of the body are named with reference to their shape, action, structure, etc.; *e.g.*, deltoid, flexor, penniform, etc. In different localities a group of muscles having a common function is named in accordance with the kind of motion it produces or to which it gives rise: *e.g.*, groups of muscles which alternately diminish or increase the angular distance between two bones are known respectively as flexors and extensors; such muscle groups are usually found in association with ginglymus joints. Muscles which rotate the bone to which they are attached around its own axis without producing any great change of position are known as rotators, and are found in association with enarthrodial or ball-and-socket joints. Muscles which impart an angular movement to the extremities to and from the median line of the body are termed adductors and abductors respectively.

In addition to the actions of individual groups of muscles in producing special movements, in some regions of the body, several groups of muscles are coördinated for the accomplishment of certain definite functions; *e.g.*, the functions of respiration, mastication, etc. The coördination of axial and appendicular muscles enables the individual to assume certain postures, such as standing, sitting, and lying; to engage in various acts of locomotion, as walking, running, dancing, swimming.

Levers.—The function or special mode of action of individual muscles can be understood only when the bones with which they are connected are regarded as levers whose fulcra or fixed points lie in the joints where the movement takes place, and the muscles as sources of power for imparting movement to the levers with the object of overcoming resistance.

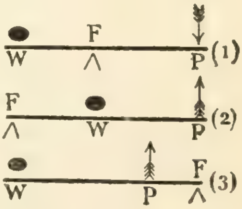


FIG. 39.—THE THREE ORDERS OF LEVERS.

In mechanics levers of three kinds or orders are recognized according to the relative positions of the fulcrum or axis of motion, the applied power, and the weight to be moved. (See Fig. 39.)

In levers of the first order the fulcrum, F, lies between the weight or resistance, W, and the power or moving force, P. The distance P F is known as the power arm and the distance W F as the weight arm. As examples of this form of lever found in the human body may be mentioned:

1. The elevation of the trunk from the flexed position. The axis of movement, the fulcrum, lies in the hip-joint; the weight, that of the trunk, acting as if concentrated at the center of gravity, which lies close to the tenth dorsal vertebra; the power, the muscles attached to the tuberosity of the ischium. The opposite movement is equally one of the first order, but the relative positions of P and W are reversed.
2. The head in its movement backward and forward on the atlas.

In levers of the second order the weight lies between the power and the fulcrum. As illustration of this form of lever may be mentioned:

1. The depression of the lower jaw, in which movement the fulcrum is the temporomaxillary articulation; the resistance, the tension of the elevator muscles; the power, the contraction of the depressor muscles.
2. The raising of the body on the toes, in which movement the fulcrum is the toes, the weight that of the body acting through the ankle, the power the gastrocnemius muscle applied to the heel bone.

In levers of the third order the power is applied at a point lying between the fulcrum and the weight. As example of this form of lever may be mentioned:

1. The flexion of the forearm, in which the fulcrum is the elbow-joint, the power the biceps and brachialis anticus muscles applied at their points of insertion, the weight that of the forearm and hand.
2. The extension of the leg on the thigh.

When levers are employed in mechanic operations, the object aimed at is the overcoming of a great resistance by the application of a small force acting through a great distance, so as to obtain mechanic advantage. In the mechanism of the human body the reverse generally obtains, viz., the overcoming of a small resistance by the application of a large force acting through a short distance. As a result there is a gain in the extent and rapidity of the movement of the lever. The power, however, owing to its point of application, acts at a great mechanic disadvantage in many instances, especially in levers of the third order.

Postures.—Owing to its system of joints, levers, and muscles the human body can assume a series of positions of equilibrium, such as standing and sitting, to which the term posture has been given. In order that the body may remain in a state of stable equilibrium in any posture, it is essential that the vertical line passing through its center of gravity shall fall within the base of support.

Standing is that position of equilibrium in which a line drawn through the center of gravity of the entire body falls within the base of support. This position is maintained largely by the mechanical conditions of the joints, apparently for the purpose of reducing to a minimum muscular action, so that it can be prolonged for some time without giving rise to fatigue. In the military position, which may be assumed as the normal position, all the joints must be in such a condition of extension and fixation that the body will represent a rigid column resting on the astragalus and supported by the arch of the foot. This is accomplished:

1. By balancing the head on the apex of the vertebral column. This is done by the action of the muscles on the back of the neck. The muscular effort is, however, very slight, as the center of gravity of the head lies but a short distance in front of the articulation.

2. By making the vertebral column erect and rigid. This is brought about by the action of the common extensor muscles of the trunk. In this condition the center of gravity lies just in front of the tenth dorsal vertebra. The head, trunk, and upper extremities are now supported by the hip-joints; and in order that this support may give to the body a certain degree of stable equilibrium, independent of muscular action, the line of gravity falls behind the line uniting the center of rotation of the two joints. In consequence the body would fall backward were it not prevented by the tension of the iliofemoral ligament and the fascia lata.

The line of gravity, continued downward, passes through the knee-joint posterior to the axis of rotation, and hence the body would now fall backward were it not prevented by the tension of the lateral ligaments and the contraction of the quadriceps femoris muscle. Though the body is supported by the astragalus, the line of gravity does not pass through the line uniting the two joints, for in so doing constant muscular effort would be required to maintain stable equilibrium; passing a short distance in advance of this line, there would be a tendency of the body to fall forward, which is prevented by the extensor muscles of the foot. When the body is in the erect or military position, the center of gravity lies between the sacrum and last lumbar vertebra. Standing is thus an act of balancing, and requires not only the static conditions of joints, but the dynamic conditions of various groups of muscles, and hence is not a position of absolute ease and cannot be maintained for any length of time without experiencing discomfort and fatigue. Sitting erect is an attitude of equilibrium in which the body is balanced on the tubera ischii, when the head and trunk together form a rigid column.

Locomotion is the act of transferring the body as a whole through space, and is accomplished by the combined action of its own muscles. The acts involved consist of walking, running, jumping, etc.

Walking is a complicated act involving almost all the voluntary muscles of the body either for purposes of progression or for balancing the head and trunk, and may be defined as a progression in a forward horizontal direction due to the alternate action of both legs. In walking one leg becomes for the time being the active or supporting leg, carrying the trunk and head; the other the passive but progressing leg, to become in turn the active leg when the foot touches the ground. Each leg is therefore alternately in an active and in a passive state.

Running is distinguished from walking by the fact that at a given moment both feet are off the ground and the body is raised in the air.

THE VISCERAL OR INVOLUNTARY MUSCLE

The **visceral muscle,** as the name implies, is found in the walls of hollow viscera, where it is arranged in the form of a membrane or sheet. It is present in the walls of the alimentary canal, blood-vessels, respiratory tract, ureter, bladder, vas deferens, uterus, fallopian tubes, iris, etc. In some situations it is especially thick and well developed—*e.g.*, uterus and pyloric end of the stomach; in others it is thin and slightly developed.

The Histology of the Visceral Muscle-fiber.—When examined with the microscope, the muscle sheet is seen to be composed of fibers, narrow, elongated, and fusiform in shape. As a rule, they are extremely small, measuring only from 40 to 250 micromillimeters in length and from 4 to 8 micromillimeters in breadth. The center of each fiber presents a narrow, elongated nucleus. The muscle-protoplasm which makes up the body of the fiber appears to be enclosed by a delicate elastic membrane resembling in some respects the sarcolemma of the skeletal muscle. In some animals the visceral fiber presents a longitudinal striation suggesting the existence of fibrillæ surrounded by sarcoplasm (Fig. 40). The fibers are united longitudinally and transversely by a cement material. The muscle is increased in thickness by the superposition of successive layers. At varying intervals the fibers are grouped into bundles or fasciculi by septa of connective tissue (Fig. 41). Blood-vessels ramify in the connective tissue and furnish the necessary nutritive material.

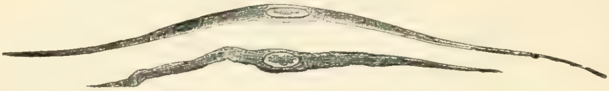


FIG. 40.—TWO SMOOTH MUSCLE-FIBERS FROM SMALL INTESTINE OF FROG. × 240. Isolated with 35 per cent. potash-lye. The nuclei have lost their characteristic form through the action of the lye.—(*Stöhr.*)

The visceral muscle receives stimuli from the spinal cord, not directly, however, as in the case of the skeletal muscle, but indirectly through the intermediation of ganglion cells, which may be located at some distance from the muscle or near the walls of the viscera. Non-medullated fibers from the ganglion pass directly into the muscle, where they frequently unite to form a general plexus. From this plexus fine branches take their origin and ultimately become physiologically associated with the muscle-fiber.

Physiologic Properties.—The visceral muscles which have been subjected to experiment are mainly those of the stomach, intestine, bladder, ureter, and iris. From the results of the experiments which have been published, it is evident that all visceral muscles possess elasticity, tonicity, irritability, and conductivity.

The **elasticity** of the bladder muscle of the cat was strikingly shown in the experiments published by Dr. Colin C. Stewart. When this muscle was weighted with weights differing by a common increment, it was extended on the addition of each weight, though to a progressively less extent. On the removal of the weights the muscle eventually returned to its former length. The records of the extension were similar to, if not identical with, those of the skeletal muscle.

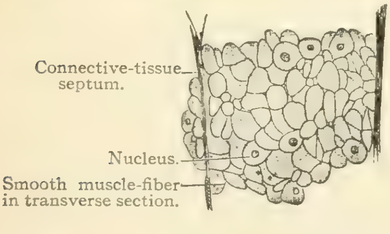

Connective-tissue septum.
Nucleus.
Smooth muscle-fiber in transverse section.

FIG. 41.—SECTION OF THE CIRCULAR LAYER OF THE MUSCULAR COAT OF THE HUMAN INTESTINE.—(*Stöhr.*)

The **tonicity** of visceral muscles is as pronounced in many situations as is the tonicity of skeletal muscles. Each muscle is continuously in a state of contraction intermediate between that of complete contraction and that of relaxation. In how far this is due to local and inherent causes or to stimuli reflected from the nervous system as a result of peripherally acting causes is not in individual instances readily determinable. From time to time the tonicity varies, increasing and decreasing in response to these various stimuli and in accordance with the functional activities of the organs in which the muscle is found.

The **irritability** manifests itself by a change of form, and doubtless by the liberation of heat on the application of any form of stimulus—mechanic, chemic, thermic, electric.

The **conductivity** is less marked in the visceral than in the skeletal muscle, and, contrary to what is observed in the latter, the conduction extends laterally as well as longitudinally from fiber to fiber. This is shown by stimulation of the exposed intestine. Shortly after the stimulus is applied the muscle contracts longitudinally—*i.e.*, in a direction at right angles to the long axis of the intestine, partially obliterating its lumen. From this point the conduction process indicated by the contraction wave passes in opposite directions for some distance along the canal. As to whether this is accomplished by protoplasmic processes extending from fiber to fiber, or whether the uniting membrane differs in conducting power from the sarcolemma, is as yet a matter of doubt. From the fact that the upper two-thirds of the ureter, though free of nerve-cells, exhibits lateral conduction, it is evident that it may take place independent of the nervous system.

The Contraction of the Visceral Muscle.—The general character of the contraction may be witnessed on opening the abdomen of a recently killed animal, especially the rabbit. Shortly after exposure to the air the walls of the intestine begin to contract in a most vigorous manner. The contraction wave beginning at various points is propagated in both directions, running along the intestinal wall for a variable distance. A succession of similar waves may be observed for some minutes. To the alternate contraction and relaxation of the muscle-fibers, which are circularly arranged, the term peristalsis is usually given. The excised stomach of a dog kept under suitable conditions will exhibit similar movements. The same holds true of the bladder muscle of the cat, the muscle of the ureter, etc. Careful observation shows a certain periodicity in the movements. Inasmuch as the cause is not apparent, these contractions are termed spontaneous or automatic.

Graphic Record of the Contraction.—For experimental purposes narrow transverse sections of the stomach of the frog or the entire bladder muscle of the cat, excised or *in situ*, according to the method of Prof. Colin C. Stewart, may be employed. If kept moist, they will retain their irritability for some hours. The changes of form may be recorded with the usual muscle lever. When thus prepared, the muscle may exhibit for several hours a series of pulsations, rhythmic in character. With spontaneously acting mammalian muscle the contraction and relaxation periods are of equal duration. With the amphibian muscle they are of unequal duration, as a rule. In both classes of animals the character of the record, a succession of large and small contractions, would indicate that the general rhythmic movement is compounded of two or three secondary rhythms which differ in rate and character. A single pulsation may be recorded by stimulating the bladder muscle with the induced or the make and break of the constant current. A curve of such a contraction is shown in Fig. 42. The contraction takes place more rapidly than the relaxation; the two phases occupying five and thirty-five seconds respectively. The latent period covered 0.25 second. With other muscles the time relations are slightly different. Tetanization of the bladder muscle of the cat occurred when the stimuli succeeded each other with a certain rapidity; the interval between stimuli approximating a period somewhat less than two seconds. This muscle responds to variations in temperature, to strength of stimulus, to the load, in a manner similar to, if not identical with, the skeletal muscle.

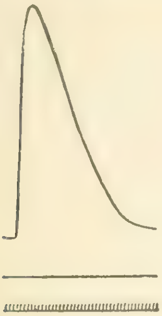


Fig. 42.—The Curve of Contraction of the Bladder Muscle at Body-temperature in Response to a Single Induction Current. The time is indicated in seconds.—(*Stewart.*)

The Function of the Visceral Muscle.—In a general way it may be said that the visceral muscle determines and regulates the passage through the viscus or organ of the material contained within it. The food in the stomach and intestines is subjected to a churning process by the muscles, in consequence of which the digestive fluids are more thoroughly incorporated and their characteristic action increased. At the same time the food is carried through the canal, the absorption of the nutritive material promoted, and the indigestible residue removed from the body. The blood is delivered in larger or smaller volumes according to the needs of the tissues through a relaxation or contraction of the muscle-fibers of the blood-vessels. The urine is forced through the ureter and from the bladder by the contraction of their respective muscles. The mode of action of the individual muscles will be described in successive chapters.

Ciliary Movement.—The free surface of the epithelium covering the mucous membrane in certain regions of the body is characterized by the presence of delicate filamentous processes termed cilia. (See Fig. 43.) Ciliated epithelium is found in man and mammals generally, in the nose, Eustachian tube, larynx, with the exception of the vocal membranes, trachea and bronchial tubes as far as the pulmonary lobules, Fallopian tubes, uterus, and epididymis. The lumen of the central canal of the spinal cord and the cavities of the brain are lined, especially in childhood, by cells provided with similar cilia. Ciliated epithelium is also found in all classes of animals, and especially in the invertebrates.

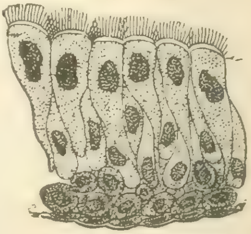


Fig. 43.—Ciliated Epithelium.

The cilia found in the human body vary in length from 0.003 mm. to 0.005 mm. They are apparently structureless and colorless, and appear to have their origin in and to be a prolongation of a transparent material on the outer surface of the cell material. The number of cilia present on the surface of any individual cell varies approximately from five to twenty-five. When ciliated epithelial cells, freshly removed from the mucous membrane and moistened with normal saline, are examined with the microscope, it will be found that the cilia are in continuous and rapid vibratile movement, so much so that the individual cilium cannot be distinguished. In time, however, their vitality declines and the rapidity of movement diminishes. When the movement of the individual cilium falls to about eight or ten per second, its character can be readily determined. It will then be seen that the movement is, as a rule, alternately a backward and a forward one, the cilium lowering and then raising itself, the latter taking place more quickly and energetically than the former. As the cilium raises itself it becomes somewhat flexed in a direction corresponding to that of the general movement. The movement, however, varies in character in different situations and in different animals. The cause of the movements and the mechanism of their coördination are unknown. They are, as far as known, independent of the nerve system. The force of ciliary motion is very great. A load of twenty grams can be supported and carried forward by the cilia on the mucous membrane of the mouth and esophagus of the frog. The activity of the cilia is associated with the nutrition of the cell of which they are a part and rises and falls with it. Experimentally it has been found that the rate and energy of the movement are greatest at a temperature of about 35° to 40°C., especially if they are bathed with normal saline, rendered slightly alkaline. Low temperatures, acids, alkalies, carbon dioxid, etc., retard the movement.

The function of the cilia, though not always apparent, is associated with the function of the passages in which they are found. As the surfaces of these passages are swept by a current of considerable power, it is probable that they assist in the passage of the materials which ordinarily traverse them. Mucus and particles of dust are carried upward through the air-passages; the ovarian cell is carried from the ovary toward the uterus; the spermatozoa, as well as the fluid in which they are contained, are carried forward through the epididymis ducts.

CHAPTER VIII

THE GENERAL PHYSIOLOGY OF NERVE-TISSUE

The Nerve-tissue.—The nerve-tissue, which unites and coördinates the various organs and tissues of the body and brings the individual into relationship with the external world, is conventionally arranged in two systems, termed the *encephalospinal* or *cerebrospinal* and the *sympathetic.*

The **encephalospinal system** consists of:

1. The brain and spinal cord, contained within the cavities of the cranium and the spinal column respectively, and
2. The cranial and spinal nerves.

The **sympathetic system** consists of:

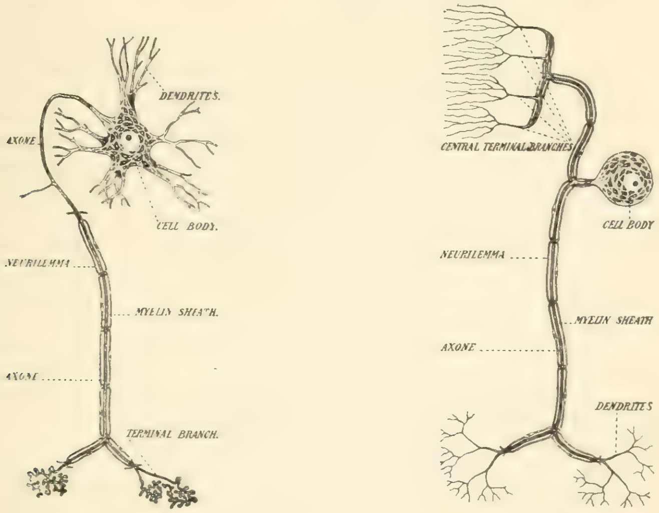
1. A chain of ganglia situated on each side of the spinal column and extending from the base of the skull to the tip of the coccyx.
2. Various collections of ganglia situated in the head, face, thorax, abdomen, and pelvis. All these ganglia are united by an elaborate system of intercommunicating nerves, many of which are connected with the cerebrospinal system. (See Chapter XXVI.)

HISTOLOGY OF NERVE-TISSUE

The Neuron.—The nerve-tissue has been resolved by the investigations of modern histologists into single morphologic units, to which the term neurons has been applied. The entire nerve system has been shown to be but an aggregate of an infinite number of neurons, each of which is histologically distinct and independent. Though having a common origin, as shown by embryologic investigations, they have acquired a variety of forms in different parts of the nerve system in the course of development. The old conception that the nerve system consisted of two distinct histologic elements, nerve-cells and nerve-fibers, which differed not only in their mode of origin, but also in their properties, their relation to each other, and their functions, has been entirely disproved.

The neuron, or neurologic unit, is histologically a nerve-cell, the surface of which presents a greater or less number of processes in varying degrees of differentiation. As represented in Fig. 44, A, the neuron may be said to consist of: (1) The nerve-cell, neurocyte, or corpus; (2) the axon, or nerve process; (3) the end-tufts, or terminal branches. Though these three main histologic features are everywhere recognizable, they exhibit a variety of secondary features in different situations in accordance with peculiarities of function.

The Nerve-cell.—The nerve-cell, or body of the neuron, presents a variety of shapes and sizes in different portions of the nerve system. Originally ovoid in shape, it has acquired, in course of development, peculiarities of form which are described as pyramidal, stellate, pear-shaped, spindle-shaped, etc. The size of the cell varies considerably, the smallest having a diameter of not more than 10 to 12 micro-millimeters, the largest not more than 150 micro-millimeters. Each cell consists of granular, striated cytoplasm, containing a distinct vesicular nucleus and a well-defined nucleolus. A characteristic feature of the cytoplasm is the presence of granules first described by Nissl, which stain deeply with methylene blue and other dyes. For this reason these granules are spoken of as chromophile granules. The remainder of the cytoplasm is penetrated in various directions with nerve fibrils which are continuous with similar fibrils running through the axonic process as well as the dendrites. The physiologic significance of Nissl's granules is unknown. The nerve fibrils are probably connected with the transmission of nerve impulses. A cell membrane has not been observed. From the surface of the adult cell portions of the cytoplasm are projected in various directions, which portions, rapidly dividing and subdividing, form a series of branches, termed *dendrites* or *dendrons*. In some situations the ultimate branches of the dendrites present short oclateral presses, known as *lateral buds*, or *gemmules*, which impart to the branches a feathery appearance. This characteristic is common to the cells of the cortex of the cerebrum and of the cerebellum. The ultimate branches of the dendrites, though forming an intricate feltwork, never anastomose with one another nor unite with dendrites of adjoining cells. According to the number of axons, nerve-cells are classified as monaxonic, diaxonic, polyaxonic. Most of the cells of the nerve system of the higher vertebrates are monaxonic. In the ganglia of the posterior or dorsal roots of the spinal and cranial nerves, however, they are diaxonic. In this situation the axons, emerging from opposite poles of the cell, either remain separate and pursue opposite directions, or unite to form a common stem, which subsequently divides into two branches, which then pursue opposite directions. (See Fig. 44, B.) The nerve-cell maintains its own nutrition, and presides over that of the dendrites and the



A. B.

FIG. 44.—A. EFFERENT NEURON; B, AFFERENT NEURON. FOUND IN BOTH SPINAL AND CRANIAL NERVES.

axon as well. If the latter be separated in any part of its course from the cell, it speedily degenerates and dies.

The Axon.—The axon, or nerve process, arises from a cone-shaped projection from the surface of the cell, and is the first outgrowth from its cytoplasm. At a short distance from its origin it becomes markedly differentiated from the dendrites which subsequently develop. It is characterized by a sharp, regular outline, a uniform diameter, and a hyalin appearance. In structure, the axon appears to consist of fine fibrillæ embedded in a clear, semi-fluid material, the neuroplasm. The axon varies in length from a few millimeters to one meter. In the former instance the axon, at a short distance from its origin, divides into a number of branches, which form an intricate feltwork in the neighborhood of the cell. In the latter instance the axon continues for an indefinite distance as an individual structure. In its course, however, especially in the brain and spinal cord, it gives off a number of *collateral* branches, which possess all its histologic features. The long axons serve to bring the body of the cell into direct relation with peripheral organs, or with more or less remote portions of the nerve system, thus constituting association or commissural fibers. Physiologic investigations have established the fact that the axon is the conducting agent of the nerve impulses.

The Myelin.—At a short distance from the cell the more or less elongated axon becomes invested with nucleated oblong cells, which subsequently become modified and constitute the medullary or myelin sheath. When fresh the myelin is clear and semi-fluid; when treated with various reagents it becomes opaque and imparts a white appearance to nerves. The function of the myelin is unknown. All axons that possess a myelin investment are known as *myelinated nerve-fibers*.

The Neurilemma.—The myelin in many situations is enclosed by a thin transparent elastic membrane known as the neurilemma. In the spinal cord and brain, the nerve fibers are for the most part wanting in this membrane.

At intervals of about seventy-five times its diameter, the medullated nerve-fiber undergoes a remarkable diminution in size, due to an interruption of the medullary substance, so that the neurilemma lies directly on the axis-cylinder. These constrictions, or *nodes of Ranvier*, taking their name from their discoverer, occur at regular intervals along the course of the nerve, separating it into a series of segments. The portion between the nodes is termed the internodal segment. It has been suggested that in consequence of the absence of the myelin at these nodes, a free exchange of nutritive material and decomposition products can take place between the axis-cylinder and the surrounding plasma. Beneath the neurilemma in each internodal segment there is a large nucleus surrounded by a small amount of granular protoplasm.

The End Tufts.—The end-tufts or terminal organs are formed by the splitting of the axon into a number of filaments, which remain independent of one another and are free from the myelin investment. The histologic peculiarities of the terminal organs vary in different situations, and in many instances are quite complex and characteristic. In peripheral organs, as muscles, glands, blood-vessels, skin, mucous membrane, the tufts are in direct histologic and physiologic connection with their cellular elements. In the brain and spinal cord the tufts are in more or less intimate relation with the dendrites of adjacent neurons.

The neurons in their totality constitute the neuron or nerve tissue. From the fact that they are arranged both serially and collaterally into a regular and connected whole, they collectively constitute a system known as the *neuron* or *nerve* system.

The neurons composing the spinal and cranial nerves are represented in Fig. 44, which are connected peripherally by their terminal branches with muscles on the one hand and with epithelium of skin, mucous membrane, etc., on the other hand. In the spinal cord the terminal branches of the afferent neuron come into histologic and physiologic relation with the dendrites of a second neuron, the axonic process of which in many instances ascends the cord to different levels or even as far as the brain, where its terminal branches come into relation with the dendrites of still another neuron, the axonic process of which is in turn connected with neurons in the cortex of either the cerebrum or cerebellum. The surfaces of the body are thus brought into relation with the cerebral and cerebellar neurons. The neurons arranged in this serial manner constitute the afferent side of the nerve system.

In a similar way the efferent neurons of the spinal and cranial nerves are brought into relation with the cortex of the cerebrum. Large pyramidal-shaped neurocytes situated in specialized regions of the cortex of the cerebrum send their axonic processes down through the brain and cord. As they approach their destination the terminal branches become related histologically and physiologically with the dendrites of the neurons composing the cranial and spinal nerves. The cortex of the cerebrum is thus brought into relation with the general musculature of the body. The neurons arranged in this serial manner constitute the efferent side of the nerve system.

Neurons, moreover, are grouped into more or less complexly organized masses, termed organs, which in accordance with their locations may be divided for convenience into central and peripheral organs.

The Central Organs of the Nerve System.—The central organs consist of the encephalon and spinal cord, contained within the cavities of the head and spinal column respectively. They consist of neurons arranged in a very complex manner. In a subsequent chapter the anatomic arrangement of their constituent parts will be detailed.

The Peripheral Organs of the Nerve System.—These consist of the cranial and spinal nerves and the sympathetic ganglia. Each nerve consists of a variable number of nerve-fibers united into firm bundles by connective tissue which supports blood-vessels and lymphatics. The bundles are technically known as *nerve-trunks* or *nerves*.

The nerve-trunks connect the brain and cord with all the remaining structures of the body. Each nerve is invested by a thick layer of lamellated connective tissue, known as the *epineurium*. A transverse section of a nerve shows (see Fig. 45), that it is made up of a number of small bundles of fibers, each of which possesses a separate investment of connective tissue—the *perineurium*. Within this membrane the nerve-fibers are supported by a fine stroma—the *endoneurium*. After pursuing a longer or shorter course, the nerve-trunk gives off branches, which interlace very freely with neighboring branches, forming plexuses, the fibers of which are distributed to associated organs and regions of the body. From their origin to their termination, however, nerve-fibers retain their individuality, and never become blended with adjoining fibers.

As nerves pass from their origin to their peripheral terminations, they give off a number of branches, each of which becomes invested with a lamellated sheath—an offshoot from that investing the parent trunk. This division of nerve-bundles and sheath continues throughout all the branchings down to the ultimate nerve-fibers, each of which is surrounded by a sheath of its own, consisting of a single layer of endothelial cells. This delicate transparent membrane, the sheath of Henle, is separated from the nerve-fiber by a considerable space, in which is contained lymph destined for the nutrition of the fiber. Near their ultimate terminations the nerve-fibers themselves undergo division, so that a single fiber may give origin to a number of branches, each of which contains a portion of the parent axis-cylinder and myelin.

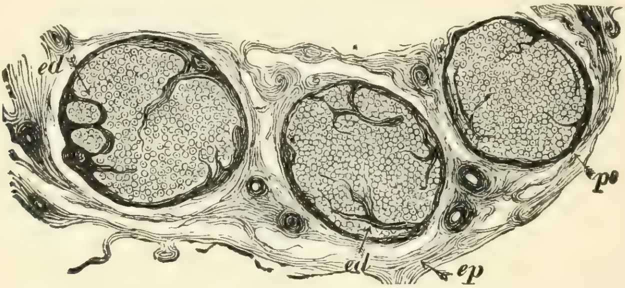


FIG. 45.—TRANSVERSE SECTION OF A NERVE (MEDIAN). *ep.* Epineurium. *pe.* Perineurium. *ed.* Endoneurium.—(*Landois and Stirling.*)

Sympathetic Ganglia.—A sympathetic ganglion consists essentially of a connective-tissue capsule with an interior framework. The meshes of this framework contain nerve-cells possessing dendrites and branching axons. The majority of the axons are devoid of myelin and are therefore known as non-myelinated nerve-fibers. Owing to the absence of the myelin they present a rather pale or grayish appearance. In all instances, with the exception of the ganglion cells of the heart, the axons are distributed to non-striated muscle tissue and to the epithelium of glands.

The nerve-cells of the ganglia are also in histologic connection with the terminal branches of certain fine medullated nerve-fibers which leave the spinal cord by way of the ventral roots of the spinal nerves. These nerve-fibers are designated *pre-ganglionic* fibers, while those emerging from the cells are designated *post-ganglionic* fibers.

Blood-supply.—Nerves being parts of living cells require for the maintenance of their nutrition a certain amount of blood. This is furnished by the blood-vessels ramifying in and supported by the connective-tissue framework. Here as elsewhere there is a constant exchange, through the capillary wall and the neurilemma, of nutritive material to the nerve proper and of waste materials to the blood.

The Chemic Composition and Metabolism.—Chemic analysis of nerve-tissue has shown the presence of water, proteins (two globulins, a nucleo-protein and neurokeratin), certain lipoids, *e.g.*, (a) cholesterin (a monotomic alcohol free from both nitrogen and phosphorus), (b) several cerebrosides or galactosides (nitrogen-holding bodies, free from phosphorous, compounds of a glucoside character, as shown by their yielding on hydrolysis the reducing carbohydrate galactose), (c) phosphatids (compounds containing both nitrogen and phosphorus, *e.g.*, lecithin, kephalin, sphingo-myelin), inorganic salts, and a series of nitrogen-holding bodies such as creatin, xanthin, urea, leucin, etc. As to the metabolism that is taking place in nerve-cells and fibers, practically nothing definite is known. That such changes, however, are taking place would be indicated first by the blood-supply, and second by the fact that withdrawal of the blood-supply is followed by a loss of irritability. The metabolism of the central organs of the nerve system is more active and extensive. In this situation any withdrawal of blood from compression or occlusion of blood-vessels is followed by impairment of nutrition and loss of function.

THE RELATION OF THE PERIPHERAL ORGANS OF THE NERVE SYSTEM TO THE CENTRAL ORGANS

Spinal Nerves.—The nerves in connection with the spinal cord are thirty-one in number on each side. If traced toward the spinal column, it will be found that the nerve-trunk passes through an intervertebral foramen. Near the outer limits of the foramina each nerve-trunk divides into two branches, generally termed roots, one of which, curving slightly forward and upward, enters the spinal cord on its anterior or ventral surface, while the other, curving backward and upward, enters the spinal cord on its posterior or dorsal surface. The former is termed the anterior or ventral root; the latter, the posterior or dorsal root. Each dorsal root presents near its union with the ventral root a small ovoid grayish enlargement known as a ganglion. Both roots previous to entering the cord subdivide into from four to six fasciculi.

A microscopic examination of a cross-section of the spinal cord shows that the fibers of the ventral roots can be traced directly into the body of the nerve-cells in the ventral horns of the gray matter. The fibers of the dorsal roots are not so easily traced, for they diverge in several directions shortly after entering the cord. In their course they give off collateral branches which, in common with the main fiber, end in tufts which become associated with nerve-cells in both the ventral and dorsal horns of the gray matter.

Cranial Nerves.—The nerves in connection with the base of the brain are known as cranial nerves; some of these nerves present a similar ganglionic enlargement, and therefore may be regarded as dorsal nerves, while others may be regarded as ventral nerves. Their relations within the medulla oblongata are similar to those within the spinal cord.

Efferent and Afferent Nerves.—Nerves are channels of communication between the brain and spinal cord, on the one hand, and the skeletal muscles, glands, blood-vessels, visceral muscles, skin, mucous membrane, etc., on the other. Some of the nerve-fibers serve for the transmission of nerve energy from the brain and spinal cord to certain peripheral organs, and so accelerate or retard, augment or inhibit their activities; others serve for the transmission of nerve energy from certain peripheral organs to the brain and spinal cord which gives rise to sensation or other modes of nerve activity. The former are termed *efferent* or *centrifugal*, the latter *afferent* or *centripetal* nerves. Experimentally it has been determined that the anterior or ventral roots contain all the *efferent* fibers, the posterior or dorsal roots all the *afferent* fibers.

The Peripheral Endings of Nerves.—The efferent nerves as they approach their ultimate terminations lose both the neurilemma and myelin sheaths. The axon or axis-cylinder then divides into a number of branches which become directly and intimately associated with tissue-cells. The particular mode of termination varies in different situations. These terminations are generally spoken of as end-organs, terminal organs, or end-tufts.

In the *skeletal* muscle the nerve-fiber loses both neurilemma and myelin sheath at the point where it comes in contact with the muscle-fiber. After penetrating the sarcolemma, the axon or axis-cylinder divides into a number of small branches which appear to be embedded in a relatively large mass of sarcoplasm and nuclei, the whole forming the so-called "motor plate." Each muscle-fiber possesses one such plate or end-organ in mammalia, several in the frog. (Fig. 46.)

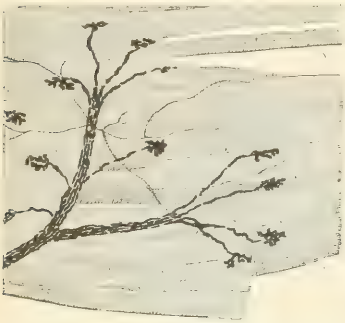


Fig. 46.—Motor Nerve-endings of Intercostal Muscle-fibers of a Rabbit. × 150.—(*Stöhr.*)

In the *visceral* muscle the terminal nerve-fibers derived from sympathetic or peripheral neurons are primarily non-medullated. The axons divide and subdivide and form plexuses which surround the muscle-cell bundles. Fine fibers from the plexuses are given off which ultimately come into relation with each individual cell, on the surface of which they terminate in the form of one or more granular masses.

In the *glands*, taking as an illustration the parotid and mammary glands, the nerve-fibers, also derived from sympathetic or peripheral neurons, pass into the body of the gland and ultimately reach the acini, on the outer surface of which they ramify and form a plexus. From this plexus fine fibers penetrate the acinus wall and end on the gland-cell. The fibers present a varicose appearance (Fig. 47).

The afferent nerves as they approach their ultimate terminations undergo similar changes. The end-tufts become associated, in some situations, with specialized end-organs which are extremely complex.

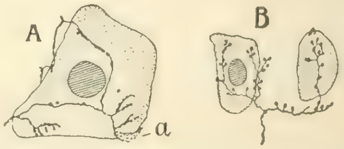


Fig. 47.—Terminations of Nerve-fibers in the Gland-cells. A. Cell of the parotid gland of a rabbit. B. Cells of the mammary gland of a cat in gestation.—(*Doyon and Morat.*)

In the *skin* and *mucous* membranes the mode of termination varies considerably. The following are some of the principal modes:

1. Free endings in the epithelium.
2. Tactile cells of Merkel.
3. Tactile corpuscles in the papillæ of the true skin.
4. Pacinian corpuscles found attached to the nerves of the hands and feet, to the intercostal nerves, and to nerves in other situations.
5. End-bulbs of Krause in the conjunctiva, clitoris, penis, etc.

(A consideration of these end-organs will be found in the chapters devoted to the organs of which they form a part.)

In the *skeletal muscles* afferent fibers become associated with small spindle-shaped structures known as *muscle-spindles* or *neuromuscle* end-organs. These spindles vary in length from 1 mm. to 4 mm. They consist of a capsule of fibrous tissue containing from five to twenty muscle-fibers. After penetrating the several layers of the capsule, the nerve-fibers lose the neurilemma and myelin sheaths. The axons or axis-cylinders then divide into several long narrow branches which wind themselves in a spiral manner around the contained muscle-fiber and terminate in small oval-shaped discs. Similar endings have been observed in the tendons of muscles.

Development and Nutrition of Nerves.—The **efferent nerve-fibers,** which constitute some of the cranial nerves and all the ventral roots of the spinal nerves, have their origin in cells located in the gray matter beneath the aqueduct of Sylvius, beneath the floor of the fourth ventricle, and in the ventral horns of the gray matter of the spinal cord. These cells are the modified descendants of independent, oval, pear-shaped cells—the neuroblasts—which migrate from the medullary tube. As they approach the surface of the cord their axons are directed toward the ventral surface, which eventually they pierce. Emerging from the cord, the axons continue to grow, and become invested with the myelin sheath and neurilemma, thus constituting the ventral roots. (Fig. 48.)

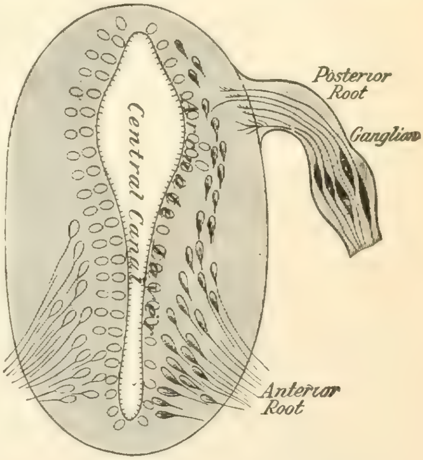


Fig. 48.—Diagram Showing the Mode of Origin of the Ventral and Dorsal Roots.—(*Edinger, after His.*)

The **afferent nerve-fibers,** which constitute some of the cranial nerves and all the dorsal roots of the spinal nerves, develop outside of the central nerve system and only subsequently become connected with it. (See Fig. 48.) At the time of the closure of the medullary tube a band or ridge of epithelial tissue develops near the dorsal surface, which, becoming segmented, moves outward and forms the rudimentary spinal ganglia. The cells in this situation develop two axons, one from each end of the cell, which pass in opposite directions, one toward the spinal cord, the other toward the periphery. In the adult condition the two axons shift their position, unite, and form a **T**-shaped process, after which a division into two branches again takes place. In the ganglia of all the sensori-cranial and sensori-spinal nerves the cells have this histologic peculiarity.

The efferent fibers are therefore to be regarded as outgrowths from the nerve-cells in the ventral horns of the gray matter, and serve to bring the cells into anatomic and physiologic relationship directly with the skeletal muscles and indirectly, through the intermediation of ganglia (see sympathetic nerve system), with visceral muscles, blood-vessels, and glands.

The afferent fibers are to be regarded as outgrowths from the cells of the dorsal nerve ganglia, and serve to bring the skin, mucous membrane, and certain visceral structures into relation with specialized centers in the central nerve system.

Nerve Degeneration.—If any one of the cranial or spinal nerves be divided in any portion of its course, the part in connection with the periphery in a short time exhibits certain structural changes, to which the term degeneration is applied. The degenerative process begins simultaneously throughout the entire course of the nerve, and consists in a disintegration and reduction of the myelin and axis-cylinder into nuclei, drops of myelin, and fat, which in time disappear through absorption, leaving the neurilemma intact. Coincident with these structural changes there is a progressive alteration and diminution in the excitability of the nerve. From these facts it has been assumed that the nerve-cells exert over the entire course of the nerve-fibers a nutritive or a trophic influence. This idea has been greatly strengthened since the discovery that the axis-cylinder, or the axon, has its origin in and is a direct outgrowth of the cell. When separated from the parent cell, the fiber appears to be incapable in itself of maintaining its nutrition.

It has for a long time been stated that the portion of the divided nerve in connection with the brain or spinal cord retains its normal condition with the exception of a few millimeters at its peripheral end. This statement has been disproved by recent observations which show that the cell body and its attached axon also in the course of time undergo an atrophy which may become permanent; also that the chromatin material of the cell, Nissl's granules, undergo dissolution and no longer stain with the usual dyes, a condition which may last for two weeks or more. In some instances the granules may be restored. These degenerative changes in the nerve cell are probably the result of the cessation of its customary function.

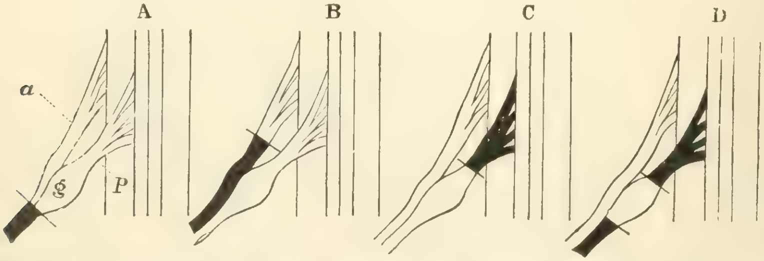


FIG. 49.—DEGENERATION OF SPINAL NERVES AND NERVE-ROOTS AFTER SECTION. A, Section of nerve-trunk beyond the ganglion. B, Section of ventral root. C, Section of dorsal. D. Excision of ganglion. *a*. Ventral root. *p*. Dorsal root. *g*. Ganglion.—(*Dalton.*)

The relation of the nerve-cells to the nerve-fibers, in reference to their nutrition, is demonstrated by the results which follow section of the ventral and dorsal roots of the spinal nerves. If the ventral root alone be divided the immediate degenerative process is confined to the peripheral portion, the central portion remaining for a variable period normal. If the dorsal root be divided on the peripheral side of the ganglion, degeneration takes place only in the peripheral portion of the nerve. (See Fig. 49.) If the root be divided between the ganglion and the cord, degeneration takes place only in the central portion of the root. From these facts it is evident that the trophic centers for the ventral and dorsal roots lie in the spinal cord and spinal nerve ganglia, respectively, or, in other words, in the cells of which they are an integral part. The structural changes which nerves undergo after separation from their centers are degenerative in character, and the process is usually spoken of, after its discoverer, as the *Wallerian degeneration.*

When the nerve-cells from which the nerve-fibers arise, whether efferent or afferent, undergo degeneration from any cause whatever, the nerve-fiber becomes involved in the degenerative process and when it is completed the structures to which they are distributed, especially the muscles, undergo an atrophic or fatty degeneration, with a change or loss of their irritability. This is, apparently, not to be attributed merely to inactivity, but rather to a loss of nerve influences, inasmuch as inactivity merely leads to atrophy and not to degeneration.

Reunion and Regeneration.—When a nerve-trunk is divided there is a loss of function of the parts to which it is distributed, and usually involves both motion and sensation. This, however, is not necessarily permanent, for after a variable period of time it not infrequently happens that the functions are restored because of a reunion of the separated ends and a regeneration of the peripheral portion. A histologic study of the nerve-fibers after separation from the nerve-cells shows that coincidently with the degenerative process there occurs a regenerative process, consisting in a multiplication of the nuclei lying just beneath the neurilemma and an accumulation around them of a granular protoplasm which in due time completely fill the neurilemma. At this stage the fiber is known as a band-fiber. If now the physical conditions are such as to permit of a reunion of the nerve, this takes place, and under the nutritive influence of the cell the axis-cylinder grows into the band-fiber and the protoplasm becomes transformed into myelin as in the original fiber. The axis-cylinder continues to grow and extend itself forward until it reaches its ultimate termination.

CLASSIFICATION OF NERVES

The Efferent Nerves.—The efferent nerves may be classified, in accordance with their distribution and the characteristic forms of activity to which they give rise, into several groups, as follows:

1. *Skeletal-muscle* or *motor* nerves, those which convey nerve energy or nerve impulses directly to skeletal-muscles and excite them to activity.
2. *Gland* or *secretor* nerves, those which convey nerve impulses to glands by way of ganglia and influence in one direction or another the degree of their activity. Those which cause the formation and discharge of the secretion peculiar to the gland, are known as secreto-motor, while those which decrease or inhibit the secretion are known as secreto-inhibitor nerves.
3. *Vascular* or *vaso-motor* nerves, those which convey nerve impulses to the muscle-fibers of the blood-vessels and change in one direction or the other the degree of their natural contraction. Those which increase the contraction are known as vaso-constrictors or vaso-augmentors; those which decrease the contraction are known as vaso-dilatators or vaso-inhibitors. The nerves which pass to that specialized part of the vascular apparatus, the heart, transmit nerve impulses which on the one hand accelerate its rate or augment its force, and on the other hand

inhibit or retard its rate and diminish its force. For this reason they are termed cardiac nerves, one set of which is known as cardio-accelerator and cardio-augmentor, the other as cardio-inhibitor nerves.

4. *Visceral* or *viscero-motor* nerves, those which transmit nerve impulses to the muscle walls of the viscera and change in one direction or another the degree of their contraction. Those which increase or augment the contraction are known as viscero-augmentor, while those which decrease or inhibit the contraction, are known as viscero-inhibitor nerves.
5. *Hair bulb* or *pilo-motor* nerves, those which transmit nerve impulses to the muscle-fibers which cause an erection of the hairs.

Of the foregoing nerves the skeletal-muscle or motor nerves alone pass directly to the muscle. The gland, the vascular and the visceral nerves, all terminate at a variable distance from the peripheral organ around a local sympathetic ganglion, which in turn is connected with the peripheral organ. The former are termed pre-ganglionic. The latter post-ganglionic fibers. (See Fig. 13.)

The Afferent Nerves.—The afferent nerves may also be classified, in accordance with their distribution and the character of the sensations or other modes of nerve activity to which they give rise, into several groups, as follows:

1. *Tegumentary* nerves, comprising those distributed to skin, mucous membranes and sense organs and which transmit nerve impulses from the periphery to the nerve centers. They may be divided into reflex and sensorifacient nerves.
    A. *Reflex* nerves, those which transmit nerve impulses to the spinal cord and medulla oblongata, where they give rise to different modes of nerve activity. They may be divided into:
        1. Reflex excitator nerves, which transmit nerve impulses which cause an excitation of nerve centers and in consequence increased activity of peripheral organs, *e.g.*, skeletal muscles, glands, blood-vessels and viscera.
        2. Reflex inhibitor nerves, which transmit nerve impulses which cause an inhibition of nerve centers and in consequence, decreased activity of the peripheral organs. It is quite probable that one and the same nerve may subserve both sensation and reflex action, owing to the collateral branches which are given off from the afferent roots as they ascend the posterior column of the cord.
    B. *Sensorifacient* nerves, those which transmit nerve impulses to the brain where they give rise to conscious sensations. They may be subdivided into:
        1. Nerves of special sense—*e.g.*, olfactory, optic, auditory, gustatory, tactile, thermal, pain, pressure—which give rise to correspondingly named sensations.
        2. Nerves of general sense—*e.g.*, the visceral afferent nerves—those which give rise normally to vague and scarcely perceptible sensations, such as the general sensations of well-being or discomfort, hunger, thirst, fatigue, sex, want of air, etc.
2. *Muscle* nerves, comprising those distributed to muscles and tendons and which transmit nerve impulses from muscles and tendons to the brain where they give rise to the so-called muscle sensations, *e.g.*, the direction

and the duration of a movement, the resistance offered and the posture of the body or of its individual parts.

PHYSIOLOGIC PROPERTIES OF NERVES

Nerve Irritability or Excitability and Conductivity.—These terms are employed to express that condition of a nerve which enables it to develop and to conduct nerve impulses from the center to the periphery, or from the periphery to the center, in response to the action of stimuli. A nerve is said to be excitable or irritable so long as it possesses these capabilities or properties. For the manifestation of these properties the nerve must retain a state of physical and chemic integrity; it must undergo no change in structure or chemic composition. The irritability of an *efferent* nerve is demonstrated by the contraction of a muscle, by the secretion of a gland, or by a change in the caliber of a blood-vessel, whenever a corresponding nerve is stimulated. The irritability of an *afferent* nerve is demonstrated by the production of a sensation or a reflex action whenever it is stimulated. The irritability of nerves continues for a certain period of time after separation from the nerve-centers and even after the death of the animal, the time varying in different classes of animals. In the warm-blooded animals, in which the nutritive changes take place with great rapidity, the irritability soon disappears—a result due to disintegrative changes in the nerve, caused by the withdrawal of the blood-supply and other non-physiologic conditions. In cold-blooded animals, on the contrary, in which the nutritive changes take place relatively slowly, the irritability lasts, under favorable conditions, for a considerable time. Other tissues besides nerves possess irritability, that is, the property of responding to the action of stimuli—*e.g.*, glands and muscles, which respond by the production of a secretion or a contraction.

Independence of Tissue Irritability.—The irritability of nerves is distinct and independent of the irritability of muscles and glands, as shown by the fact that it persists in each a variable length of time after their histologic connections have been impaired or destroyed by the introduction of various chemic agents into the circulation. Curara, for example, induces a state of complete paralysis by modifying or depressing the conductivity of the end-organs of the nerves just where they come in contact with the muscles, without impairing the irritability of either nerve-trunks or muscles. Atropin induces complete suspension of gland activity by impairing the terminal organs of the secretor nerves just where they come into relation with the gland-cells, without destroying the irritability of either gland-cell or nerve.

Nerve Stimuli.—Nerves do not possess the power of spontaneously generating and propagating nerve impulses; they can be aroused to activity only by the action of an external stimulus. In the physiologic condition the stimuli capable of throwing the nerve into an active condition act for the most part on either the central or peripheral end of the nerve. In the case of motor nerves the stimulus to the excitation, originating in some molecular disturbance in the nerve-cells, acts upon the nerve-fibers in connection with them. In the case of sensor or afferent nerves the stimuli act upon the peculiar end-organs with which the sensor nerves are in connection, which in turn excite the nerve-fibers. Experimentally, it can be demonstrated that nerves can be excited by a sufficiently powerful stimulus applied in any part of their extent.

Nerves respond to stimulation according to their habitual function; thus, stimulation of a sensor nerve, if sufficiently strong, results in the sensation of pain; of the optic nerve, in the sensation of light; of a motor nerve, in contraction of the muscle to which it is distributed; of a secretor nerve, in the activity of the related gland, etc. It is, therefore, evident that peculiarity of nerve function depends neither upon any special construction or activity of the nerve itself nor upon the nature of the stimulus, but entirely upon the peculiarities of its central and peripheral end-organs.

Nerve stimuli may be divided into—

1. *General stimuli*, comprising those agents which are capable of exciting a nerve in any part of its course.
2. *Special stimuli*, comprising those agents which act upon nerves only through the intermediation of the end-organs.

The end-organs are specialized highly irritable structures placed between the nerve-fibers and the surface. They are especially adapted for the reception of special stimuli and for the liberation of energy, which in turn excites the nerve-fiber to activity.

General stimuli:

1. Mechanic: Sharp taps, sudden pressure, cutting, etc.
2. Thermic: Sudden application of heated object.
3. Chemic: Contact of various substances which alter their chemic composition quickly, *e.g.*, strong acids or alkalies, sol. sodium chlorid 15 per cent., sugar, urea, etc.
4. Electric: Either the constant or induced current.

Special stimuli:

For afferent nerves—

1. Light or ethereal vibrations acting upon the end-organs of the optic nerve in the retina.
2. Sound or atmospheric undulations acting upon the end-organs of the auditory nerve.
3. Heat or vibrations of the air acting upon the end-organs in the skin.
4. Chemic agencies acting upon the end-organs of the olfactory and gustatory nerves.

For efferent nerves—

A molecular disturbance in the central nerve-cells from which they arise, the nature of which is unknown.

Nature of the Nerve Impulse.—As to the nature of the nerve impulse generated by any of the foregoing stimuli, either general or special, but little is known. It has been supposed to partake of the nature of a molecular disturbance, a combination of physical and chemic processes attended by the liberation of energy, which propagates itself from molecule to molecule. The passage of the nerve impulse is accompanied by changes of electric tension, the extent of which is an indication of the intensity of the molecular disturbance. Judging from the deflections of the galvanometer needle it is probable that when the nerve impulse makes its appearance at any given point it is at first feeble, but soon reaches a maximum development, after which it speedily declines and disappears. It may, therefore, be graphically represented as a wave-like movement with a definite length and time duration. (See page 106.) Under strictly physiologic conditions the nerve impulse passes in one direction only; in efferent nerves from the center to the periphery, in afferent nerves from the periphery to the center. Experimentally, however, it can be demonstrated that when a nerve impulse is aroused in the course of a nerve by an adequate stimulus it travels equally well in both directions from the point of stimulation. When once started, the impulse is confined to the single fiber and does not diffuse itself to fibers adjacent to it in the same nerve-trunk.

Rapidity of Conduction of the Nerve Impulse.—The passage of a nerve impulse, either from the brain to the periphery or in the reverse direction, requires an appreciable period of time. The velocity with which the impulse travels in human sensory nerves has been estimated at about 50 meters a second, and for motor nerves at from 28 to 33 meters a second. The rate of movement is, however, somewhat modified by temperature, cold lessening and heat increasing the rapidity; it is also modified by electric conditions, by the action of drugs, the strength of the stimulus, etc. The rate of transmission through the spinal cord is considerably slower than in nerves, the average velocity for voluntary motor impulses being only 11 meters a second, for sensory impulses 12 meters, and for tactile impulses 40 meters a second.

Nerve Fatigue.—Inasmuch as nerves are parts of living cells, the seat of nutritive changes, it might be supposed that the passage of nerve impulses would be attended by the disruption of energy-holding compounds, the production of waste products, the liberation of heat, and in time by the phenomena of fatigue. Though it is probable that changes of this character occur, yet no reliable experimental data have been obtained which afford a clue as to the nature or extent of any such changes. Stimulation of motor nerves with the induced electric current for four hours appears to be without influence either on the intensity of the nerve impulse or the rate of its conduction.

Identity of Efferent and Afferent Nerves and Nerve Impulses.—Notwithstanding the classification of nerve-fibers based on differences of physiologic actions, there are no characters, either histologic or chemic, which serve to distinguish them from one another. Moreover, as the nerve impulse is conducted through a nerve-fiber equally well in both directions, as determined by experiments, it is probable that it does not differ in character in the two classes of nerves. That the efferent fibers conduct the nerve impulses from the nerve-centers to the periphery, and the afferent nerves from the periphery to the centers, is because of the fact that they receive their stimulus physiologically only in the centers or at the periphery. The fundamental reason for difference of effects produced by stimulation of different nerves is the character of the organ to which the nerve impulse is conducted. A nerve is merely the transmitter of the nerve impulse, which if conducted to a muscle excites contraction; to a gland, secretion; to a blood-vessel, variation in caliber; to special areas in the brain, sensations of light, sound, pain, etc.

Electric Excitation of Nerves.—For the purpose of studying the physiologic activities of nerves it has been found convenient to employ the nerve-muscle preparation (the gastrocnemius muscle and sciatic nerve) and to use as a stimulus the induced electric current. (See Fig. 50.) When kept moist, this preparation is extremely sensitive to either the galvanic or the induced current.

Though the development and conduction of a nerve impulse may be demonstrated by the deflection of the galvanometer needle or the movement of the mercury in the capillary electrometer, it is more conveniently demonstrated by the contraction of a muscle, the vigor of which, within limits, may be taken as a measure of the intensity of the impulse. The preparation should be enclosed in a moist chamber and the nerve connected with the inductorium through the intervention of non-polarizable electrodes. The muscle may be attached to the muscle-lever and its contractions recorded.

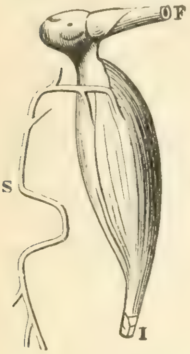


FIG. 50.—NERVE-MUSCLE PREPARATION OF A FROG. F. Femur. S. Sciatic nerve. I. Tendo Achillis. — (*Landois and Stirling.*)

A single shock of an induced current develops, it is believed, a single nerve impulse followed by a single muscle contraction. A minimal contraction following a minimal electric stimulus presupposes the development of a nerve impulse of low intensity. Within certain limits a maximal contraction following a maximal electric stimulus presupposes the development of a nerve impulse of high intensity. Intermediate contractions indicate nerve impulses of corresponding intensity.

Tetanization of a muscle indicates that the nerve impulses arrive at the muscle with a frequency so great that the muscle does not succeed in relaxing from the effect of one stimulus before the next arrives. Complete as well as incomplete tetanus may be developed by gradually increasing the frequency of the stimulus. The character of the contraction caused by indirect stimulation—*i.e.*, through the nerve—does not differ in any essential respect from that due to direct stimulation.

ELECTRIC PHENOMENA OF NERVES

Electric Currents from Injured Nerves.—It was discovered by du-Bois Reymond that electric currents can be obtained from nerves as well as from muscles, and that the electric properties of the former correspond in most respects to those of the latter. The laws governing the development and mode of action of the currents derived from muscles are equally applicable to the currents derived from nerves.

A nerve-cylinder obtained by making two transverse sections of any given nerve presents, as in the case of muscles, a natural and two artificial transverse surfaces. A line drawn around the cylinder at a point lying midway between the two end surfaces constitutes the equator. From such a cylinder strong currents are obtained when the natural longitudinal surface and the transverse surface are connected with the electrodes of the galvanometer circuit. The strength of the current thus obtained will diminish or increase according as the electrode on the longitudinal surface is removed from or brought near to the equator. If two symmetric points on the longitudinal surface equidistant from the equator are united, no current is obtainable. When asymmetric points on the longitudinal surface are connected, weak currents are obtained, in which case the point lying nearer the equator becomes positive to the point more distant, which becomes negative. From these facts it is evident that all points on the longitudinal surface are electrically positive to the transverse surface and that the point of greatest positive tension is situated near the equator (Fig. 51).

The electromotive force of the nerve current varies in strength with the length and thickness of the nerve. The strongest current obtained from the nerve of the frog is equal to the 0.002 of a Daniell cell; that obtained from the nerve of the rabbit, 0.026 of a Daniell. The existence of the nerve current, its strength, duration, etc., depend largely on the maintenance of physiologic conditions. All influences which impair the nutrition of the nerve diminish the current. With the death of the nerve all electric phenomena disappear.

Negative Variation of the Nerve Current.—During the passage of the nerve impulse the resting nerve current, or the demarcation current, diminishes more or less completely in intensity, undergoes a *negative variation*, as shown by the return of the galvanometer needle, due to a change in its electromotive condition or to a diminution of the difference in potential between the positive longitudinal and negative transverse sections. This negative variation of the demarcation current is observed equally well from either the central or peripheral end of the nerve. If the two ends of the nerve are connected with galvanometers and the nerve stimulated in the middle, the demarcation currents simultaneously undergo a negative variation. This may be taken as a proof that the excitation process propagates itself equally well in both directions. The negative variation is intimately connected with changes in the molecular condition of the nerve and is not due to any extraneous electric or other influence. And du-Bois Reymond was also enabled to obtain a negative variation of the current in the nerves of a living frog which were yet in connection with the spinal cord. In this experiment the sciatic nerve was divided at the knee and freed from its connections up to the spinal column; the transverse and longitudinal surfaces were then placed in connection with the electrodes of the galvanometer wires and the current permitted to influence the needle. The animal was then subjected to the action of strychnin. Upon the appearance of the muscle spasms the needle was observed to swing backward toward the zero point to the extent of from 1 to 4 degrees, and upon the cessation of the spasms to return to its previous position. In an experiment of this nature it is obvious that the negative variation was the result of a physiologic stimulation of the nerve arising within the spinal cord.

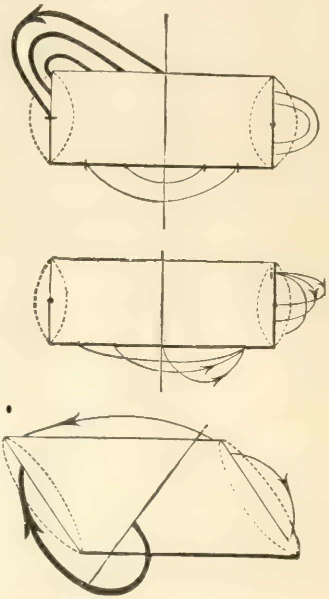


FIG. 51.—DIAGRAM TO ILLUSTRATE THE CURRENTS IN NERVES. The arrowheads indicate the direction; the thickness of the lines indicates the strength of the currents. —(*Landois and Stirling.*)

The question also here arises as to whether the negative variation is due to a steady, continuous decrease of the natural current, or whether it is due to successive and rapidly following variations in its intensity, similar to that observed in muscles. Though this cannot be demonstrated with the physiologic rheoscope, as was the case with the muscle, there can be no doubt, both from experimentation and analogy, that the latter supposition is the correct one. It has been shown that when non-polarizable electrodes connected with Siemen's telephone are placed in connection with the longitudinal and transverse sections of a nerve, low, sonorous vibrations are perceived during tetanic stimulation—a proof that the active state of the nerve is connected with the production of discontinuous electric currents. The oscillations of the mercurial column of the capillary electrometer also reveal similar electric changes. It was also demonstrated by Bernstein with a specially devised apparatus, the repeating rheotome, that the negative variation is composed of a large number of single variations which succeed each other in rapid succession and summarize themselves in their effect on the needle.

Electric Currents from Uninjured Nerves.—The pre-existence of electric currents in living and wholly uninjured nerves while at rest has also been denied by Hermann, who regards all portions of the nerve as isoelectric, any difference of potential being the result of some injury to its surface.

Action Currents.—For reasons to be stated below, it is very difficult to determine the presence of diphasic action currents during the passage of an excitatory impulse through the nerve-fiber. The so-called negative variation of the resting nerve current—the demarcation current—which is occasioned by tetanic stimulation, Hermann regards as the expression of an *action current* which flows in the nerve in a direction opposite to the demarcation current. The origin of this action current is to be sought for in the continuous negativity of that portion of the longitudinal surface of the nerve in contact with the diverting electrode, while the dying substance of the transverse surface takes no part in the excitation. This *tetanic* action current, or negative variation, was discovered by du-Bois Reymond, and Bernstein later succeeded in obtaining this action current during the passage of a single excitation process. That the return of the galvanometer needle toward the zero point is not due to an annulment of the demarcation current itself, but to the appearance of an action current, is shown by the fact that if the former be compensated by a battery current until the needle rests on the zero point the appearance of the latter current will cause the needle to swing in a direction the opposite of that caused by the demarcation current. The negative variation and action current may therefore be regarded as one and the same thing. It is the expression of the change the nerve is undergoing during the passage of the nerve impulse. The rapidity with which the negative variation or action current travels, the variation in its intensity from moment to moment, the time required for it to pass a given point, would express the change in the nerve to which the term nerve impulse is given. From experiments made with the differential rheotome, Bernstein calculated that the speed of the negative variation is about 28 meters a second; that it is at first feeble, soon rises to a maximum, and then declines; that is requires 0.0006 to 0.0008 of a second to pass a given point. From these data it is evident that the negative variation or action current has a space value of 0.0006 of 28 meters or about 18 mm. Transferring these statements to the nerve impulse, it may be said that it is a molecular disturbance, traveling at the rate of about 28 meters a second, is wave-like in character, the wave being 18 millimeters in length and occupying from 0.0006 to 0.0008 of a second in passing any given point.

Absence of Diphasic Action Currents.—When any two points on the longitudinal surface which do not exhibit a current are connected with the galvanometer and a single wave of excitation passes beneath the electrodes, it might be expected that, as in the case of the muscle, a diphasic action current would be observed, from the fact that the portions of the nerve beneath the electrodes become alternately negative with reference to all the rest of the nerve. This, however, is not the case, the absence of the two opposing phases of the action current being explained on the supposition that the negativity of the two led-off points is of equal amount, and that, owing to the great rapidity with which the excitation wave travels, the two phases fall together too closely in time to alternately influence the galvanometer needle. During stimulation of the nerve, when two currentless or isoelectric points are connected, there is also an absence of the action current, as was observed first by du-Bois Reymond, and which is to be explained on similar grounds. It is true that an apparent action current is sometimes seen when the stimulating current is very powerful or the seat of stimulation too near the diverting electrodes. This, however, must be attributed to an electrotonic state of the nerve.

The Effects of a Galvanic Current on a Nerve.—When a constant galvanic current of medium strength is made to pass through a portion of a nerve, several distinct effects are produced:

1. *The development of a nerve impulse* at the moment the current enters and at the moment the current leaves the nerve, *i.e.*, at the moment the circuit is made and at the moment it is broken. The development of the nerve impulse is made evident by the contraction of the muscle if the nerve-muscle preparation be used. If the current be either very weak, or very strong, the muscle contraction may not always take place.

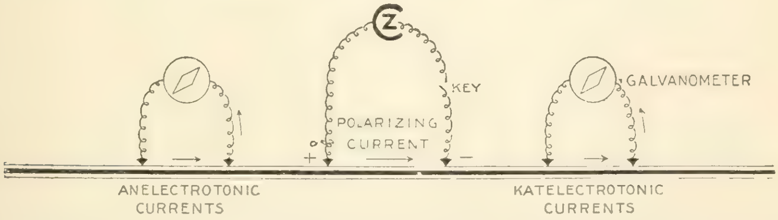


FIG. 52.—THE SITUATION AND DIRECTION OF ELECTROTONIC CURRENTS, DEVELOPED BY THE PASSAGE OF AN ELECTRIC CURRENT THROUGH A PORTION OF A NERVE.

2. *The development of electric currents* on each side of the positive pole or anode, and the negative pole or kathode (see Fig. 52), which can be led off by means of wires into a galvanometer circuit from either the artificial transverse and longitudinal surfaces, or from any two points on the longitudinal surface as shown by the deflection of the galvanometer needle. The direction of these electric currents in the nerve coincides with that of the galvanic or "polarizing current." The "natural nerve currents," the currents of injury or demarcation currents, as they are variously termed, are at the same time increased and decreased at opposite extremities of the nerve according to the direction of the polarizing current.

To this changed condition of the electromotive forces in a nerve the term electrotonus was given (du-Bois Reymond). The currents themselves are known as electrotonic currents; from their relation to the anode and kathode, they are termed anelectrotonic and katelectrotonic currents. The condition of the nerve around the poles both in the intra-polar and extra-polar regions is known as anelectrotonus and katelectrotonus.

The electrotonic currents vary considerably in strength and extent, according to the intensity of the polarizing current, increasing steadily with the intensity of the latter up to the point at which the polarizing current begins to destroy the physical and chemic integrity of the nerve. The electrotonic currents are strongest in the immediate neighborhood of the electrodes, but gradually diminish in strength as the distance between the polarized and led-off portions is increased. The distance to which the electrotonic currents extend along the nerve will depend very largely upon the strength of the polarizing current, though it is conditioned by the physical state of the nerve; for if it be ligated or injured beyond the polarized portion, the electrotonic currents are abolished. The electrotonic currents have no necessary connection with the natural nerve currents, nor are they to be regarded as branchings of the galvanic current. They are in all probability of artificial origin, due to an inner positive and negative polarization of the nerve which extends for a variable distance on each side of the poles, and due to the action of the polarizing or the galvanic current.

3. *An alteration in the excitability and conductivity* of the nerve in the neighborhood of the poles, whereby the results of nerve stimulation—that is, muscle contraction, sensation, and inhibition—are increased or decreased according to the strength and direction of the current. To this condition the term electrotonus was also given (Pflüger). This word has thus been employed to express two distinct series of effects exhibited by a nerve through a portion of which a constant galvanic current is passing. It appears desirable, for the sake of clearness, to limit the term electrotonus to the electric or electrotonic currents which can be led off from either extremity of the nerve, and to apply to the modifications of irritability which accompany electrotonus the expression, electrotonic alteration of excitability and conductivity.

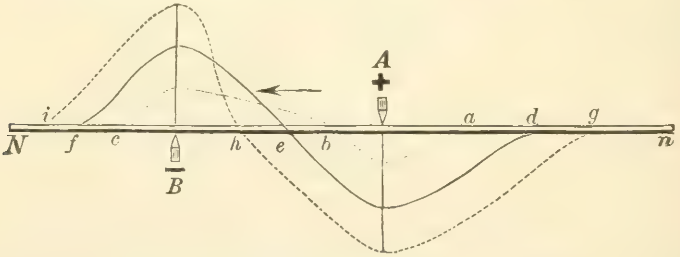


FIG. 53.—SCHEME OF THE ELECTROTONIC EXCITABILITY.—(*Landois and Stirling.*)

During the passage of the current the excitability of the intra-polar as well as the extra-polar regions undergoes a change which, as shown on examination, is found to be *diminished* in the neighborhood of the *anode* or positive pole and *increased* in the neighborhood of the *kathode* or negative pole. These alterations in the excitability are most marked in the immediate vicinity of the electrodes, though they extend for some distance into both the extra-polar and intra-polar regions, though with gradually diminishing intensity, until they finally disappear. Between the electrodes there is a point where the excitability is unchanged and known as the neutral or indifferent point (Fig. 53). The extent to which the excitability is modified as well as the position of the neutral point will depend largely on the strength of the polarizing or galvanic current.

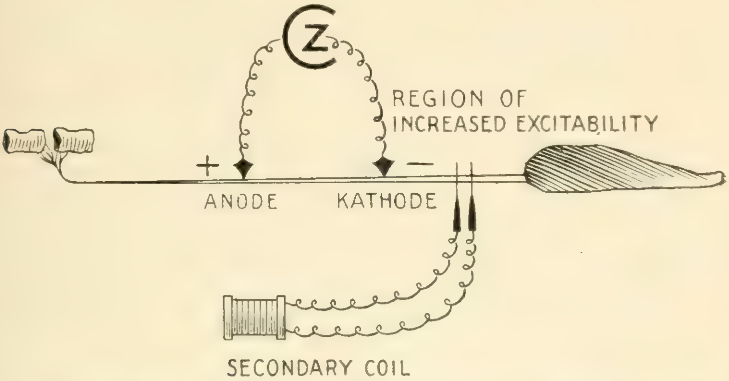


FIG. 54.—DIAGRAM SHOWING THE REGION OF INCREASED EXCITABILITY CAUSED BY THE PASSAGE OF A GALVANIC CURRENT THROUGH A PORTION OF A NERVE, STIMULATION OF WHICH GIVES RISE TO INCREASED CONTRACTION.

The electrotonic alterations of excitability and conductivity can be experimentally demonstrated on the muscle-nerve preparation in the following manner:

1. With a descending current of medium strength. Previous to the closure of the polarizing current, the nerve is stimulated first in the extra-polar anodic region and the extra-polar kathodic region with an induction shock of medium intensity and the height of the contraction recorded. On repeating the stimulation *after* closure of the polarizing current the contraction resulting from stimulation of the anodic region will be enfeebled or may be entirely wanting, while the contraction from stimulation of the kathodic region will be decidedly increased. (See Fig. 54.)

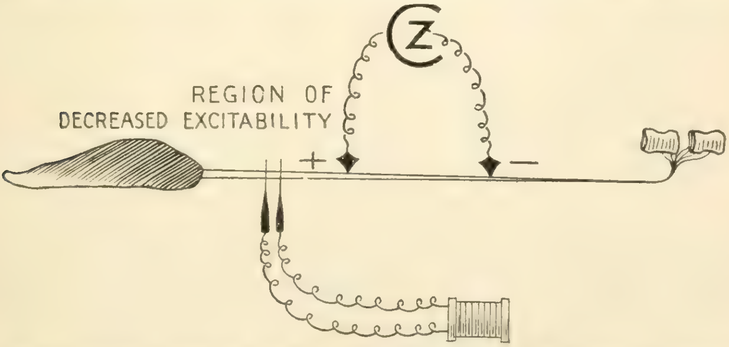


FIG. 55.—DIAGRAM SHOWING THE REGION OF DECREASED EXCITABILITY CAUSED BY THE PASSAGE OF A GALVANIC CURRENT THROUGH A PORTION OF A NERVE, STIMULATION OF WHICH GIVES RISE TO DECREASED CONTRACTION.

2. With an ascending current of the same strength. After preliminary testing of the excitability and the subsequent closure of the polarizing current, it will be found that stimulation of the extra-polar anodic region will provoke a much less energetic contraction or perhaps none at all. Stimulation of the extra-kathodic region, though of increased excitability, as shown by the previous experiment, may also fail to provoke a contraction, owing to the diminished conductivity of the region in the neighborhood of the anode. The impulse on reaching this region is blocked in its passage. A similar if not more marked decrease in the conductivity may be developed in the region of the kathode if the current strength be very great. (See Fig. 55.)

The Law of Contraction; Polar Stimulation.—It was stated in a previous paragraph that when a galvanic current of medium strength is made to enter a nerve, and when it is withdrawn from the nerve, there is a contraction of its related muscle. These are generally known as the make and break effects. During the actual passage of the current no effect is observed so long as its strength remains uniform. Any sudden variation in the strength of the current at once arouses the nerve to activity, as shown by a muscle contraction.

The muscle response to the make and break of the constant current is more or less variable unless the direction of the current as well as its strength be taken into consideration. If the current is made to flow from the central toward the peripheral end of the nerve it is termed a *direct*, *descending*, or *centrifugal* current; if it is made to flow in the reverse direction, it is termed an *indirect*, *ascending*, or *centripetal* current. The strength of the current is determined and regulated by means of a rheocord.

The make and break of currents of different but known strengths and directions give rise to contractions which occur with more or less regularity. The order in which they occur under these varying conditions of experimentation has been determined and tabulated as follows by Pflüger, and is termed the *law of contraction:*

Current intensity	Ascending current		Descending current	
	Make	Break	Make	Break
Weak	Contraction.	Rest.	Contraction.	Rest.
Medium	Contraction.	Contraction.	Contraction.	Contraction.
Strong	Rest.	Contraction.	Contraction.	Rest or weak contraction.

The results as above tabulated are sometimes complicated on the opening of the circuit by a series of irregular pulsations of the muscle, an apparent tetanus, and long known as the opening tetanus of Ritter, which is attributed to rapid changes in the irritability of the nerve, in the region of the anode. A similar tetanic contraction of the muscle is sometimes observed on the closure of the circuit due to continued excitation in the region of the kathode. This is known as the closing tetanus of Wundt or of Pflüger. All the phenomena of the law of contraction were explained by Pflüger on the assumption that the current stimulates the nerve only at the one electrode, at the *kathode on closing*, and at the *anode on opening;* or, in other words, by the appearance of katelectrotonus or by the disappearance of anelectrotonus, both conditions being attended by a rise of excitability—not, however, by the opposite changes. It is further assumed that the appearance of katelectrotonus is more effective as a stimulus than the disappearance of anelectrotonus. For these reasons the term *polar stimulation* is generally employed in discussing the make and break effects of the galvanic current. The law of contraction may then be explained as follows: Very feeble currents, either ascending or descending, produce contraction only upon the closure of the circuit, the sudden *increase of the excitability* in the *katelectrotonic area* being alone sufficient to generate an impulse. The contraction which follows the closing of the weak ascending current depends upon the fact that the decrease of excitability and conductivity at the anode is insufficient to interfere with the conduction of the kathodal stimulus. Medium currents, either ascending or descending, produce contraction both on closing and opening the circuit. The appearance of katelectrotonus and the disappearance of anelectrotonus are both sufficiently powerful to generate an impulse without, however, seriously impairing the conductivity of the nerve.

Very strong currents produce contraction only upon the opening of the ascending and closure of the descending currents, or upon the passage of the excitability in the former from the *marked anelectrotonic decrease to the normal condition*, and in the latter from the normal to that of katelectrotonic increase. The absence of contraction upon the closure of the ascending current is dependent upon the blocking of the kathodal stimulus by the decrease of the excitability and conductivity at the anode. With the opening of the descending current the disappearance of anelectrotonus should also be followed by contraction, which would indeed be the case if the stimulus so generated was not blocked by the decrease of the conductivity at the kathode in consequence of the fall of a high state of katelectrotonus to the normal condition.

The order in which the contractions occur may be tabulated as follows:

	With Ascending Current.		With Descending Current.	
Weak.............	1. K. C. C.[1]	—	K. C. C.	—
Medium..........	2. K. C. C.	A. O. C.[2]	K. C. C.	A. O. C.
Strong............	3. —	A. O. C.	K. C. C.	A. O. C.(?)

Polar Stimulation of Human Nerves.—The preceding statements as to changes in the excitability caused by the passage of a constant current, as well as to the law of contraction, are based entirely on experiments made with the isolated nerve of the frog. It is probable, however, that the same phenomena would have been observed had the nerve of a mammal been used and its excitability been maintained.

If the electrodes connected with the wires of a sufficiently strong galvanic battery be applied to the skin over the course of a superficially lying nerve, *e.g.*, the brachial, it will be found that there occurs on the closure of the circuit an *increase* in the excitability in the extra-polar anelectrotonic region and a *decrease* in the excitability in the extra-polar katelectrotonic region, as shown by stimulating the nerve in the extra-polar regions with the induced current—results which are in apparent contradiction to those obtained with the isolated nerve. This want of accordance in the results of the two classes of experiments arises from a failure to recognize the fact that the physiologic anode and kathode do not coincide with the physical anode and kathode.

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[1] K. C. C., kathodal closing contraction.

[2] A. O. C., anodal opening contraction.

It has been experimentally demonstrated that owing to the large amount of readily conducting tissue by which the nerve is surrounded, the current density, though great immediately under the electrode, quickly decreases at a short distance from it, so that for the nerve it becomes almost *nil*. The current, therefore, shortly after entering, again leaves the nerve at various points which become physiologic kathodes. Stimulation of this physiologic kathode with the induced current gives rise, therefore, to the phenomenon of increased excitability in the region of the anode. If, however, the galvanic and stimulating current be combined in one circuit and both be applied to the same tract of nerve, results will be obtained which harmonize with those obtained with the frog's nerve.

The changes in the excitability of a nerve of a living man and the contractions which follow the closing and opening of the constant current have been thoroughly studied by Waller and de Watteville. These observers employed a method similar to that of Erb, conjoining in one circuit the testing and polarizing currents. By the graphic method they recorded first the contraction produced by an induction shock alone; and, secondly the contraction produced by the same stimulus under the influence of the polarizing current. As a result of many experiments, they also demonstrated an increase of the excitability in the polar region when it is cathodic, and a decrease when it is anodic. Following the suggestion of Helmholtz, that the current density quickly decreases with the distance from the electrodes, they recognize, at the point of entrance and exit of the current from the nerve, two regions—a polar, having the same sign as the electrode, and a peripolar, having the opposite sign (Figs. 56 and 57). The peripolar regions also experience similar alterations of excitability, though less in degree, according as they are kathodic or anodic.

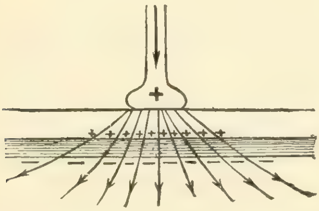

FIG. 56.—ANODE OF BATTERY. Polar region of nerve is anodic. Peripolar region of nerve is cathodic.

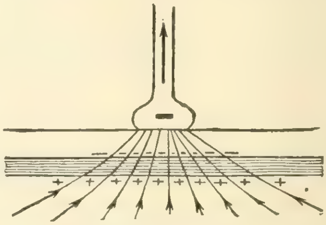

FIG. 57.—CATHODE OF BATTERY. Polar region of nerve is cathodic. Peripolar region of nerve is anodic.—(*Waller.*)

As it is impossible to confine the current to the trunk of the nerve when surrounded by living tissues, as is easily the case when experimenting with the frog's nerves, it is incorrect to speak of either ascending or descending currents. Waller,[1] who has thoroughly studied the electrotonic effects of the galvanic current from this point of view, sums up his conclusions in the following words: "We must apply one electrode only to the nerve and attend to its effects alone, completing the circuit through a second electrode, which is applied according to convenience to some other part of the body.

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[1] "Human Physiology," p. 363, 1891.

"Confining our attention to the first electrode, let us see what will happen according as it is *anode* or *kathode* of a galvanic current (Figs. 56 and 57). If this electrode be the anode of a current, the latter enters the nerve by a series of points and leaves it by a second series of points; the former, or proximal series of points, collectively constitutes the *polar* zone or region; the latter, or distal series of points, collectively constitutes the *peripolar* zone or region. In such case the polar region is the seat of entrance of current into the nerve—*i.e.*, is *anodic;* the peripolar region is the seat of exit of current from the nerve—*i.e.*, is *kathodic.* If, on the contrary, the electrode under observation be the kathode of a current, the latter enters the nerve by a series of points which collectively constitute a 'peripolar' region, and it leaves the nerve by a series of points which collectively constitute a 'polar' region. The current, at its entrance into the body, diffuses widely, and at its exit it concentrates; its 'density' is greatest close to the electrode, and, the greater the distance of any point from the electrode, the less the current density at that point; hence it is obvious that the current density is greater in the polar than in the peripolar region. These conditions having been recognized, we may apply to them the principles learned by study of frogs' nerves under simpler conditions.

"Seeing that, with either pole of the battery, whether anode or kathode, the nerve has in each case points of entrance (constituting a collective anode) and points of exit to the current (constituting a collective kathode), and admitting as proved that make excitation is kathodic, break excitation anodic, we may, with a sufficiently strong current, expect to obtain a contraction at make and at break with either anode or kathode applied to the nerve; and we do so, in fact. When the kathode is applied, and the current is made and broken, we obtain a *kathodic make contraction* and a *kathodic break contraction;* when the anode is applied, and the current is made and broken, we obtain an *anodic make contraction* and an *anodic break contraction.* These four contractions are, however, of very different strengths; the kathodic make contraction is by far the strongest; the kathodic break contraction is by far the weakest; the kathodic make contraction is stronger than the anodic make contraction; the anodic break contraction is stronger than the kathodic break contraction. Or, otherwise regarded, if, instead of comparing the contractions obtained with a sufficiently strong current, we observe the order of their appearance with currents gradually increased from weak to strong, we shall find that the kathodic make contraction appears first, that the kathodic break contraction appears last, and the formula of contraction for man reads as follows:

"Weak current........	K. C. C.			
Medium current.......	K. C. C.	A. C. C.	A. O. C.	
Strong current........	K. C. C.	A. C. C.	A. O. C.	K. O. C."

The constant or the galvanic current is frequently used for therapeutic and diagnostic purposes. In accordance with the statements above quoted, one electrode should be applied to the part to be investigated, the other to some indifferent region. The electrode conveying the current to or from this part should be of a size sufficient to localize the current and to increase its density. It was discovered by Duchenne that there are certain points all over the body stimulation of which is more quickly followed by muscle contraction than others. It was subsequently discovered by Remak that these points coincide with the entrance of the nerve into the muscle. It is to these motor points that the one electrode should be applied.

Reactions of Degeneration.—In consequence of the degeneration and changes in irritability which occur in nerves when separated from their centers and in muscles when separated from their related nerves, either experimentally or as the result of disease, the response of these structures to the induced, and the make and break of the constant current, differs from that observed in the physiologic condition. The facts observed under the application of these two forms of electricity are of importance in the diagnosis and therapeutics of the precedent lesions. The principal difference of behavior is observed in the muscles, which exhibit diminished or abolished excitability to the induced current, while at the same time manifesting an increased excitability to the constant current; so much so is this the case that a closing contraction is just as likely to occur at the positive as at the negative pole. This peculiarity of the muscle response is termed the *reaction of degeneration.* The synchronous diminished excitability of the nerves is the same for either current. The term "partial reaction of degeneration" is used when there is a normal reaction of the nerves, with the degenerative reaction of the muscles. This condition is observed in progressive muscular atrophy.

Reflex Action.—Inasmuch as many of the muscle movements of the body, as well as the formation and discharge of secretions from glands, variations in the caliber of blood-vessels, inhibition and acceleration in the activity of various organs, are the result of stimulations of the terminal organs of afferent nerves, they are termed, for convenience, reflex actions, and, as they take place for the most part through the spinal cord and medulla oblongata and independently of the brain or of volitional influences, they are also termed involuntary actions. A reflex action of skeletal muscles, glands, or non-striated muscles of blood-vessels or of viscera, therefore, may be defined as an action which takes place independent of volition and in response to peripheral stimulation. As many of the processes to be described in succeeding chapters are of this character, requiring for their performance the coöperation of several organs and tissues associated through the intermediation of the nerve system, it seems advisable to consider briefly, in this connection, the parts involved in a reflex action, as well as their mode of action. As shown in Fig. 13, page 42, the necessary structures are as follows:

1. A receptive surface, skin, mucous membrane, sense-organs, etc.
2. An afferent nerve-fiber and cell.
3. An emissive cell, from which arises—
4. An efferent nerve, distributed to a responsive organ, as
5. Skeletal muscle, gland, blood-vessel, etc.

Such a combination of structures constitutes a reflex mechanism or arc, the nerve portion of which, in the case of skeletal muscles, is composed of but two neurons—an afferent and an efferent. In the case of glands and non-striated muscles, whether of blood-vessels or viscera, the efferent neuron instead of passing direct to the responsive organ, arborizes around the nerve-cells of a peripheral sympathetic ganglion. The reflex arc is then continued by the processes of the ganglion cells. An arc of this simplicity would of necessity subserve but a simple movement. The majority of reflex activities, however, are extremely complex, and involve the coöperation and coördination of a number of nerve centers situated at different levels of the spinal cord on the same and opposite side, and of responsive organs frequently situated at distances more or less remote from one another. This implies that a number of neurons are associated in function. The transference of nerve impulses coming from a localized area of a sentient surface to emissive cells situated at different levels is accomplished by the intercalation of a third neuron situated in the gray matter which is in connection, on the one hand, with the central terminals of the afferent neuron, and, on the other hand, through its collateral branches with the dendrites of the efferent neurons situated at different levels of the cord. (Fig. 58.)

For the excitation of a reflex action it is essential that the stimulus applied to the receptive surface be of an intensity sufficient to develop in the terminals of the afferent nerve a series of nerve impulses, which, traveling inward, will be distributed to and received by the dendrites of the emissive or motor cell. With the reception of these impulses there is apparently a disturbance of the equilibrium of its molecules, a liberation of energy, and, in consequence, a transmission outward of impulses through the efferent nerve to muscle, gland, or blood-vessel, separately or collectively, with the production of muscle contraction, a secretion, vascular dilatation or contraction, etc. The reflex actions take place, for the most part, through the spinal cord and medulla oblongata, which, by virtue of their contained centers, coördinate the various organs and tissues concerned in the performance of the organic functions. The movements of mastication; the secretion of saliva; the muscle, gland, and vascular phenomena of gastric and intestinal digestion; the vascular and respiratory movements; the mechanism of micturition, etc., are illustrations of reflex activity.

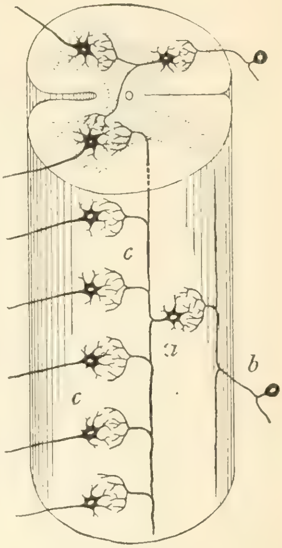

FIG. 58.—DIAGRAM SHOWING THE RELATION OF THE THIRD NEURON *a*, TO THE AFFERENT NEURON *b*, AND TO THE EFFERENT NEURONS *c*, *c*, *c*.—(*After Kölliker.*)

CHAPTER IX

FOODS

The functional activity of every organ and tissue of the body is accompanied by a more or less active disintegration of the living material, the bioplasm, of which it is composed, as well as of the food materials circulating in its interstices. The complex molecules of the living material and of the non-living food materials are continually undergoing disruption and falling into less complex and more stable compounds; these, through oxidative processes, are eventually reduced through a series of descending chemic stages to a small number of simpler compounds which, being of no further apparent value to the organism, are eliminated by the various eliminating or excretory organs, the lungs, skin, kidneys, and liver. Among these excreted compounds derived from tissue and from food metabolism the most important are urea, uric acid, and carbon dioxid. Many other compounds, organic as well as inorganic, are also eliminated from the body in the various excretions, though they are present in but small amounts. Coincident with this metabolic process there is a transformation of potential into kinetic energy, which manifests itself for the most part as heat and mechanic motion.

In order that the organs and tissues may continue in the performance of their functions, it is essential that they be supplied with nutritive materials similar to those which enter into their own composition: *viz.*, proteins, fat, carbohydrates, water, and inorganic salts. These compounds, though originally derived from the food, are immediately derived from the blood as it flows through the capillary blood-vessels. The blood is therefore to be regarded as a reservoir of nutritive material in a condition to be absorbed and transformed into utilizable and living material. Inasmuch as the materials which are lost to the body daily, through processes of disintegration and oxidation, are supplied by the blood, it is evident that this fluid would diminish rapidly in volume, with a corresponding decline in functional activity, were it not replenished by the introduction into the body of new material in the food. This is brought about by the sensations of hunger and thirst which periodically arise.

The Sensations of Hunger and Thirst.—For some time it has been supposed that hunger is a general sensation arising in consequence of nutritional changes and referred to the epigastrium. The recent experiments of Cannon, Carlson and others indicate that this is not the case, but that it arises in consequence of a contraction of the musculature of the stomach after its contents have been discharged into the intestine. By reason of the dietetic habits these hunger contractions occur three or four times a day and when once established occur on an average of about once a minute and last for about half a minute. The contractions apparently stimulate nerve endings as a result of which nerve impulses ascend to the cerebrum and evoke the sensation which is then referred to the stomach region. With the introduction of food these contractions disappear and the sensation subsides. The characteristic peristaltic contractions occurring during digestion do not give rise to the hunger sensation. The sensation of thirst arises when there is a deficiency of water in the body and is mainly referred to the mouth and fauces. With the introduction of water into the stomach and intestine and its absorption into the blood and tissues the sensation speedily disappears. The nerve mechanism by which these various results are brought about is unknown.

The foods which are consumed daily in response to sensations of hunger and thirst are complex in composition and contain, though in varying amounts, proteins, fats, carbohydrates, water, and inorganic salts, which, in contradistinction to foods, are termed food principles or, as they maintain the nutrition, nutritive principles. These compounds also contain the potential energy necessary to maintain the energy equilibrium of the body which becomes manifest as heat and mechanic motion in the transformations of the material used in the nutritive processes.

It has been stated in a previous chapter that the animal body may be regarded as a machine capable of performing each day a certain amount of work by the expenditure of a definite amount of energy. In the performance of its work, whether it be the raising of weights against gravity, or the overcoming of friction, cohesion, or elasticity, the machine suffers disintegration and metabolizes a portion of the food materials and loses a portion of its available energy. Unlike other machines, however, it possesses the power within limits of self-renewal, when supplied with foods in proper quantity and quality.

QUANTITIES OF FOOD PRINCIPLES REQUIRED DAILY

In order that the body may continue in the performance of its work and yet retain a given weight, it is essential that the loss to the body daily shall be exactly compensated by the introduction and assimilation of a corresponding amount of food principles. If this condition is realized, the body neither gains nor loses in weight, but remains in a condition of nutritive equilibrium. The determination of the extent of the metabolism is made from an analysis of the daily excretions. If therefore these are collected and analyzed, it will become possible to determine from their chief constituents the extent and character of the tissue and food metabolized, and hence to calculate the relative quantities of the different food materials necessary to replace the materials metabolized. Thus of the constituents the urea and other nitrogen-holding compounds contained in the urine and feces represent the proteins metabolized; the carbon dioxid and water represent the fat and carbohydrates metabolized. Therefore it becomes possible to determine approximately at least, from the amounts of the urea and carbon dioxid eliminated, the different amounts of the food principles required to restore the nutritive equilibrium under any given condition. As the activity of the nutritive changes varies in accordance with age, weight, climatic conditions, work done, etc., and as the excreted products vary in the same ratio, it is obvious that the required amounts of food will vary in accordance with these varying conditions, if nutritive equilibrium is to be maintained.

A Metabolism Experiment.—An experiment designed to determine the character and the extent of the chemic transformations which tissue and food materials undergo in their transit through the body is termed a metabolism experiment. It consists primarily in placing an animal under conditions that permit of the collection of all the excretions for purposes of analysis, the object of which is to deduce from the amounts of urea and other nitrogen-holding compounds, and of carbon dioxid excreted, or better, the total nitrogen and carbon they contain (1) the amount of tissue materials metabolized, during a fasting period of longer or shorter duration and hence from the nitrogen and carbon to calculate approximately, at least, the amounts of the food principles and their ratio one to another that must be returned to the body if nutritive equilibrium is to be restored; or (2) to deduce from the total nitrogen and carbon excreted, the amounts of protein, fat, and carbohydrates metabolized, that were contained in the customary foods during an experimental period. If the outcome from the body balances the income the weight of the animal remains stationary from which it is assumed that the amounts consumed constitute a normal diet. Experiments having these objects in view are made possible by enclosing the animal or man in a suitable chamber (Fig. 60) in which there is some provision for collecting the urine and feces, and to which, in addition, there is attached an apparatus for the absorption of water and carbon dioxid, both of which are caused to pass from the chamber through the absorption apparatus under the action of an aspirating pump. Simultaneously fresh air is introduced into the chamber after passing through another absorption apparatus by which it is freed from water and carbon dioxid. As the apparatus is traversed constantly by a column of air of normal composition and the waste products removed as rapidly as discharged, the experiment can be continued from six to twenty hours or more without detriment to the subject of the experiment. Previous to the beginning of the experiment the animal and the absorption apparatus are carefully weighed. At the end of the experiment the urine and feces are collected, weighed and analyzed for their chief

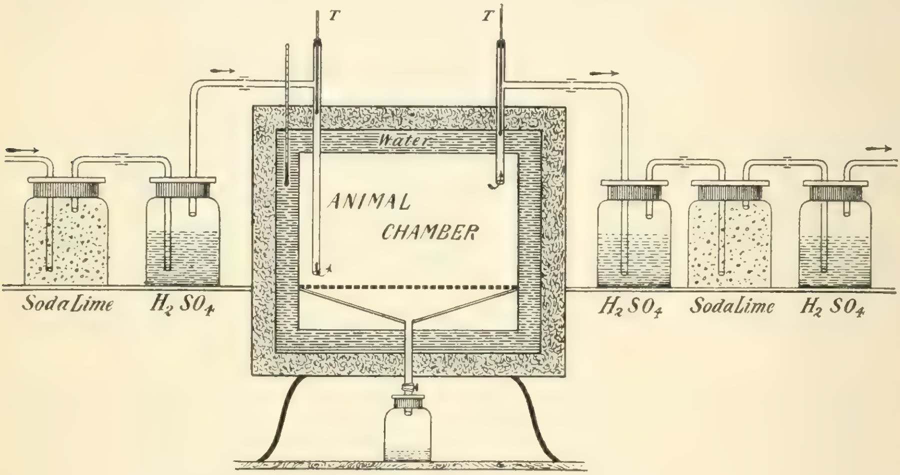

FIG. 60.—A RESPIRATION CALORIMETER.

constituent and their amounts determined. The absorption apparatus is again weighed. The increase in weight represents the amounts of water and carbon dioxid eliminated and absorbed. The animal is again weighed and the loss in weight noted.

If at the same time it is desired to collect the heat dissipated from the body it is necessary to surround the animal chamber with a water jacket, the rise in temperature of which, expressed in calories, indicates the amount of heat dissipated and collected. Since an apparatus of this character determines the extent of the respiratory exchange as well as the amount of heat dissipated, it is termed a Respiration Calorimeter.

For long-continued experiments on animals of large size and on man, one of the larger and more accurately constructed forms of apparatus, such as Benedict's (see Chapter on Animal Heat) must be employed.

In an experiment to determine the extent of the metabolism during a fasting period there was collected on the first and second days 12.17 and 12.84 grams of nitrogen and 188.5 and 179.4 grams of carbon respectively. From these amounts it was calculated that 76.1 and 80.3 grams of protein and 206.1 and 191.6 grams of fat respectively were metabolized. From these figures it is evident that at least equal amounts of protein and fat must be consumed. As a matter of fact, however, these amounts would be insufficient to maintain the energy equilibrium of the body. It has been estimated that at least from 10 to 14 per cent. more food must be added.

In an experiment made by Vierordt on the customary diet the following results, somewhat rearranged were obtained. On the right, under the term outcome, are arranged the amounts of the substances eliminated; on the left, under the term income, the amounts of the food and tissue principles which were calculated to have been metabolized. If the body is to retain its usual weight it is evident that equivalent amounts of these food principles must be introduced into the body.

COMPARISON OF THE INCOME AND OUTCOME

Income	Grams	Outcome		Grams
Protein	120	Water		3114.00
Fat	90	Urinary Solids	Salts	26.00
Carbohydrates	330		Urea	33.80
Salts	32		Extractive	6.00
Water	2818	Feces		44.00
Oxygen	744	Carbon dioxid		910.00
	4134			4134.00

In the foregoing experiment the total nitrogen contained in the urine which was 15.8 grams is expressed in the table in terms of urea. The chemic composition of urea, COH_4N_2 taken in connection with the amount stated, indicates that it is the chief end-product of protein metabolism; and as 1 gram of nitrogen corresponds to 2.14 grams of urea and either to 6.25 grams of protein it is apparent that the urinary nitrogen corresponds to 98.80 grams of protein metabolized. The feces, however, contained 3.3 grams of nitrogen corresponding to 20.62 grams of protein, making a total approximately of 120 grams of protein. From this it is apparent that an equal amount of protein would have to be introduced into the body in order to restore protein or nitrogen equilibrium.

The carbon dioxid excreted was 910 grams, equal to 248.8 grams of carbon.[1] The chemic composition of carbon dioxid, together with the amount stated, indicates that it is the chief end-product of the metabolism of fat or carbohydrate, or both, and hence from the amount eliminated it is possible to determine in terms of fat or carbohydrate the amounts that would have to be introduced into the body to restore carbon or fat and carbohydrate equilibrium. As 1 gram of C corresponds to 3.66 grams of CO_2 and either to 1.31 grams of fat it is apparent that the carbon, 184 grams, or carbon dioxid, 676 grams, eliminated corresponds to 242 grams of fat metabolized; again as 1 gram of C or 3.66 grams of CO_2 corresponds to 2.25 grams of starch, it is apparent that the carbon or carbon dioxid eliminated corresponds to 416 grams of starch. From these figures it is evident that an equal amount of fat or starch would have to be introduced into the body to restore the carbon or the fat or carbohydrate equilibrium, an amount which in either case would be larger than could be readily disposed of by the digestive apparatus and the assimilative capacities. Since the carbon dioxid comes from both fat and starch or sugar, it is difficult to determine the percentage that comes from the metabolism of the fat and the percentage that comes from the carbohydrate. From observation of the dietetic habits in different countries and of the results of metabolism experiments, it has been deemed advisable to apportion the fat to the carbohydrates in the ratio of 1 to 3.5 to 1 to 7. In the foregoing table Vierordt regarded 90 grams of fat and 330 grams of starch sufficient to restore the losses sustained.

The carbon dioxid excreted also indicates the amount of oxygen utilized in the oxidation of the carbon and the surplus hydrogen of the fats and hence the amount of oxygen that must have been absorbed from the air in the lungs. The amount of oxygen stated in the table is, however, mainly an inference and determined by deducting the loss in weight of the subject of the experiment from the combined weight of the CO_2 and the water eliminated. The salts are balanced to a greater or less degree, day by day, by the salts introduced in the foods. The excess of water discharged, 296 grams, beyond that taken into the body arises from the union of oxygen with the surplus hydrogen of the fats.

The following balance table, as given by Ranke, shows the relation of the nitrogen to the carbon in the average mixed diet and in the excretions of a man weighing 70 kilograms, in a condition of nutritive equilibrium:

Income	Grams	N.	C.	Outcome	Grams	N.	C.
Protein	100	15.5	53.0	Urea	31.5	14.4	6.16
Fat	100	......	79.0	Uric acid	0.5		
Carbohydrates	250	......	93.0	Feces		1.1	10.84
				CO_2			208.00
		15.5	225.0			15.5	225.00

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[1] It must be remembered however that of the CO_2 eliminated a portion arises from the oxidation of the carbon-holding residue of the protein, an amount in this experiment of approximately 64 grams, which would yield 234 grams of CO_2. The remainder of the CO_2, 676 grams, arose from the oxidation of the fat and carbohydrate ingested.

From the foregoing considerations it is essential that the constituents of a normal diet should be present in certain amounts and should bear a certain ratio one to another. Many attempts have been made to construct a suitable diet for a man weighing 70 kilos while doing light or moderate work. The following are accepted estimates:

	Ranke. Grams.	Voit. Grams.	Moleschott. Grams.	Atwater. Grams.	Hultgren. Grams.
Protein	100	118	130	125	134
Fat	100	56	84	125	79
Starch	250	500	550	400	522

From the foregoing estimates it is assumed that for the maintenance of nitrogen equilibrium an amount of protein, 100 grams or more, or about 1.5 to 1.7 grams for each kilogram of body weight must be consumed each day; and that if the amount falls below this minimum the tissues will be called upon to yield up a portion of their protein and thereby undergo deterioration with a consequent loss of their efficiency.

It has, however, been established that nitrogen equilibrium can be maintained without apparent detriment to the body or its activities, for a variable period of time, extending over months and years, on a diet much poorer in its protein content than in any of the foregoing diets. Chittenden has demonstrated by a long series of carefully conducted experiments on human beings, that the protein intake can be reduced to 60 grams or 0.85 grams for each kilogram of body weight without any impairment in the working capacity of the tissues or of the individual. Even this amount is in actual excess of the tissue needs as the protein metabolism according to Chittenden's experiments probably does not amount to more than 0.75 gram for each kilogram of body weight.

The daily observations of some twenty-four individuals who were placed on a diet in which the protein content was low for a period varying from five to eighteen months revealed the fact that they not only maintained the nitrogen equilibrium, but that they gained in weight and strength as shown by their capacity to meet successfully various endurance tests. These experiments would therefore indicate that the consumption of 100 or more grams of protein each day is unnecessary and that any amount beyond that actually needed for tissue repair, approximately 60 grams or even less for an individual weighing 70 kilograms is undesirable, for, as will be stated in subsequent pages, all protein when metabolized yields a series of nitrogen-holding bodies which must be subsequently eliminated by the kidneys and perhaps the intestinal glands as well. This necessitates on the part of the kidneys, the chief eliminating organs, the expenditure of a certain amount of energy. The wear and tear of these organs will be proportional to the amount of urea and other materials which they are called upon to excrete and if the kidneys fail to excrete them, some may become deposited in the tissues and give rise to certain nutritional disorders. Any unnecessary consumption of proteins should therefore be avoided.

It must be remembered, however, as protein yields energy when metabolized, that the heat value of the excluded protein must be balanced by an increase in the amount of either starch or fat or both, an increase that will yield on oxidation an equivalent amount of heat.

An advantage to the body which a high protein diet (100 to 125 grams) has over a low protein diet (60 to 80 grams) lies in the fact that the former has a greater stimulating effect on the general metabolic process than the latter as shown by an increase in the heat produced and dissiqated from the body. This action of protein is to be attributed, however, to the action of some of the amino-acids set free during digestion and subsepuently found circulating in the tissue fluids. In this situation they stimulate, by reason of their chemic features, the activity of the tissue cells, whereby their power to metabolize carbohydrates or fats is considerably increased. The experiments of Lusk have shown that when amino-acids, *e.g.*, glycocoll, alanin, etc., are administered singly or combined to an animal, there is an increase in heat production far beyond that which would result from oxidation of the carbonaceous radical (glucose) which arises in the metabolism of the amino-acids themselves; from this fact the inference is drawn that the increase in metabolism, expressed in terms of heat, which follows the ingestion of meat is to be attributed to the mass action of the absorbed amino-acids on the tissue cells. For this reason proteins are said to have a *specific dynamic action* on metabolism presumably beneficial.

CLASSIFICATION OF FOOD PRINCIPLES

Though the food principles are grouped as proteins, fats, carbohydrates, etc., the members of each group differ somewhat in chemic composition, digestibility, and nutritive value. These groups are as follows:

1. PROTEINS

Principle.	Where found.
Myosin	Flesh of animals.
Albumin, vitellin	White of egg, yolk of egg.
Caseinogen	Milk.
Serum albumin, fibrin	Blood contained in meat.
Gliadin and glutinin	Grain of wheat and some other cereals.
Vegetable albumin	Soft-growing vegetables.
Legumin	Peas, beans, lentils, etc.

2. FATS

Animal fats	In adipose tissue of animals.
Vegetable oils	In seeds, grains, nuts, fruits, and other vegetable tissues.

3. CARBOHYDRATES

Dextrose or grape-sugar	In fruits.
Levulose or fruit-sugar	
Lactose or milk-sugar	Milk.
Saccharose or cane-sugar	Sugar-cane, beet roots.
Maltose	Malt and malted foods.
Starch	Cereals, tuberous roots, and leguminous plants.
Glycogen	Liver, muscles.

4. INORGANIC

Water	In nearly all animal and vegetable foods.
Sodium and potassium chlorid	
Sodium, potassium, and calcium phosphates and carbonates	
Iron	

5. VEGETABLE ACIDS

Citric, tartaric, acetic, malic	In fruits and vegetables.

6. ACCESSORY FOODS

Coffee, Tea, Cocoa, Condiments, Spices, Alcohol.

THE DISPOSITION OF THE FOOD PRINCIPLES

The Proteins.—The protein principles of the food while in the alimentary canal undergo a series of disintegrative changes by virtue of which they are reduced in part to simple nitrogen-holding bodies, monoamino- and diamino-acids and ammonia, and in part to their immediate antecedents peptids and polypeptids, after which they are absorbed from the intestinal contents. It has for some time been assumed that in the act of absorption, the amino-acids and their immediate antecedents, are combined and transformed into the form of protein characteristic of blood and tissue fluids, viz., plasma albumin. This compound was looked upon as the immediate source of the protein necessary for tissue growth and repair. The manner in which the plasma albumin was transformed into the protein characteristic of each tissue has never been satisfactorily determined. Recently evidence has been adduced which makes it probable that the amino-acids undergo no change in the act of absorption but enter the blood as such and are carried direct to the tissues. On reaching any given tissue the cells absorb and synthesize, perhaps under the influence of an enzyme, such amino-acids as they may need for their growth and repair. The surplus amino-acids, *i.e.*, those not utilized in the synthesis of tissue protein, may be synthesized to plasma-albumin, or stored unchanged or be deaminized, *i.e.*, separated perhaps by the action of an enzyme, into the amino-group, NH_2, and some carbonaceous radical. The amino-group is then combined with hydrogen, and subsequently with carbon dioxid, to form ammonium carbonate which is then transformed into urea, a transformation that takes place to some extent in the muscles (Folin); the carbonaceous remainder may be transformed into fat or sugar, which is subsequently oxidized thus contributing to the production of heat. In the process of tissue metabolism the protein molecule undergoes disintegration and gives rise to amino-acids, the different elements of which may undergo changes similar to those just stated. The ammonia absorbed from the intestine is changed to ammonium carbonate carried direct to the liver and transformed into urea.

The Fats.—The fat principles while in the alimentary canal also undergo a series of changes whereby they are reduced by enzymic action to soap and glycerin, under which forms they are absorbed. During the act of absorption the soap and glycerin are synthesized to human fat. The fine particles thus formed in the intestinal wall are carried by the lymph vessels to the thoracic duct, and thence into the blood stream, from which they rapidly disappear. Though it is possible that a portion of the fat enters directly into the formation of the living material in general, it is generally believed that it is at once oxidized and reduced to carbon dioxid and water with the liberation of energy. The natural supposition that a portion of the synthesized fat is directly stored up in the cells of the areolar connective tissue, thus giving rise to adipose tissue, has been a subject of much controversy, though modern experimentation renders this very probable. The body-fat, under physiologic conditions, is mainly, however, a product of the transfomation of carbo-hydrates.

The question has again been raised as to whether the fine granules of emulsified fat can be absorbed without undergoing this preliminary cleavage into fat acids and glycerin. The evidence adduced in support of this view is conflicting and for its settlement further experimental work is necessary.

The Carbohydrates.—Carbohydrate principles are reduced during digestion to simple forms of sugar, chiefly dextrose and levulose. Under these forms they are absorbed into the blood. These compounds are then carried to the liver and to the muscles where they are dehydrated and stored under the form of starch, termed animal starch or glycogen. Subsequently glycogen is transformed by hydration to sugar, after which it is oxidized to carbon dioxid and water. The intermediate stages through which sugar passes before it is reduced to carbon dioxid and water are only imperfectly known. Though a large part of the carbohydrate material is at once oxidized, it is now well established that another portion contributes to the formation of, if it is not directly converted into, fat. As the carbohydrates form a large portion of the food, they contribute materially to the liberation of energy.

The Inorganic Principles.—The inorganic principles, though apparently not playing as active a part in the metabolism of the body as the organic, are nevertheless essential to its physiologic activity.

Water is promptly absorbed after ingestion and becomes a part of the circulating fluids—blood and lymph. In the digestive apparatus it favors the occurrence of those chemic changes in the food necessary for their absorption, it promotes absorption of the food, holds various constituents of the blood and other fluids in solution, hastens the general metabolism of the body, holds in solution various products of metabolic activity, and, leaving the body through the excretory organs, promotes their elimination.

Sodium chlorid is absorbed into the blood and, unless taken in excess, is utilized in replacing that which is lost to the organism daily. The exact rôle which sodium chlorid plays in the nutritive process is unknown; but, as it is present as a necessary constituent in all the fluids and solids of the body, and as it is instinctively employed as a condiment, it may be assumed to have a more or less important function.

When taken as a condiment, it imparts sapidity to the food and excites the flow of the digestive fluids; it ultimately furnishes the chlorin for the hydrochloric acid of the gastric juice. Judging from the impairment of the nutrition as observed in animals after deprivation of salt for a long period of time, it favorably influences the growth and functional activity of all tissues.

It is well known that herbivorous animals, races of men as well as individuals who live largely on vegetable foods, require a larger additional amount of sodium chlorid than carnivorous animals or human beings who live largely on animal foods, even though the two classes of foods contain relatively the same amounts. The explanation is that the vegetable foods contain potassium salts which, meeting in the blood with sodium chlorid, undergo decomposition into potassium chlorid and sodium carbonate or phosphate, all of which, when in excess, are at once eliminated by the kidneys. The blood, therefore, becomes poorer in sodium chlorid, one of its necessary constituents.

Potassium phosphate and *carbonate* are also essential to the normal composition of the solids and fluids. They impart a certain degree of alkalinity to the blood and lymph, one of the conditions necessary to the life and activity of the tissue-cells bathed by them. When administered in small doses, they increase the force of the heart, raise the arterial pressure and increase the activity of the circulation.

Calcium phosphate and *carbonate* are partly utilized in maintaining the solidity of the bones and teeth, replacing the amount metabolized daily. Inasmuch as the metabolism of these two tissues is slight, there is not much need in the adult for lime as an article of food. In young animals lime is essential to the solidification and development of bone. When deprived of it, the skeleton undergoes a defective development similar to the pathologic condition known as rickets. Lime is present in milk to the extent of 0.15 per cent., as well as in eggs and peas in relatively large quantities.

Iron is contained in both animal and vegetable foods, not, however, in the form of inorganic iron, nor in the form of an organic salt, but as a compound with nuclein, thus forming an integral part of the proteid molecule. After absorption the iron is utilized in the formation of the coloring-matter of the blood-corpuscles—hemoglobin. The organic compounds of iron and the nucleins have been termed *hematogens*. The amount of iron ingested has been estimated at 10 to 90 milligrams daily, the larger part of which is eliminated in the feces. The relatively small part eliminated by the kidneys and liver is usually taken as the amount metabolized, though it is probable that this is not wholly true, as there is evidence that iron can be retained in the body and utilized again in the formation of new hemoglobin. Contrary to what might be expected, milk contains but a very small quantity of iron not more than 3 or 4 milligrams in 1000 grams (human milk)—an amount insufficient for the development of the necessary hemoglobin. This is compensated for, however, by the accumulation of iron in the liver during intrauterine life. According to Bunge, the liver of a newly born rabbit contains as much as 18.2 milligrams per 100 grams of body-weight, while at the end of twenty-four days it contains only 3.2 milligrams per 100 grams of body-weight.

Vegetable acids increase the secretions of the alimentary canal, and are apt, in large amounts, to produce flatulence and diarrhea. After entering into combination with bases to form salts, they stimulate the action of the kidneys and promote a greater elimination of all the urinary constituents. In some unknown way they influence nutrition; when deprived of these acids, the individual becomes scorbutic.

The Accessory Foods.—The accessory foods—coffee, tea, and cocoa—when taken in moderation have a stimulating influence on the nervous system, as shown by the removal of both mental and physical fatigue, by an increased capacity for sustained mental work, and by the persistent wakefulness among those unaccustomed to their use. Coffee more especially increases the frequency and force of the heart-beat, raises the arterial pressure, and hastens the general blood-flow. It has no influence either in the way of increasing or decreasing protein metabolism.

Tea frequently acts as an astringent on the alimentary canal on account of the tannin which passes into the water when the infusion is made. Inasmuch as tannin also coagulates peptones, the excessive use of tea as a beverage is apt to derange the digestive organs and the general process of digestion.

Cocoa is more nutritive than either coffee or tea, on account of the large amount of fat and protein it contains. It is, however, less stimulating.

The active principles in coffee, tea, and cocoa, and to which their effects are to be attributed, are *caffein*, *thein*, and *theobromin* respectively. These alkaloids are chemically closely related one to the other and to the compound xanthin. They are present in the coffee seeds, the tea leaves, and the cocoa bean to the extent of 1.7 per cent., 1.4 per cent., and 1.6 per cent. respectively. When prepared as a beverage, however, there is three times as much caffein in coffee as thein in tea.

Alcohol when taken in small quantities stimulates the digestive glands to increased activity and thus promotes digestive power. Its absorption into the blood is followed by increased action of the heart, dilatation of the cutaneous blood-vessels, a sensation of warmth, and an excitation of the brain. In large quantities it acts as a paralyzant, depressing more especially the vaso-constrictor nerve-centers and certain areas of the brain, as shown by an impairment in the power of sustained attention, clearness of judgment, and muscle coördination.

Alcohol is undoubtedly oxidized in the body, as only about 2 per cent. can be obtained from the urine and expired air. It thus contributes to the store of the body-energy. Whether for this reason it can be regarded as a food—that is, whether it can be substituted in part at least for fat or carbohydrate material without impairing the protein metabolism—is at present a subject of experimentation and discussion. According to some investigators, alcohol does not retard protein metabolism, for when it is introduced into the body in amounts equivalent to the carbohydrates withdrawn from the food there is at once a rise in the amount of nitrogen excreted. Hence it cannot be regarded as a food. According to other investigators, alcohol retards or protects protein metabolism just as effectually as an equivalent amount of starch or sugar. Many more experiments are required to decide this question. When taken habitually in large quantities, alcohol deranges the activities of the digestive organs, lowers the body temperature, impairs muscle power, lessens the resistance to depressing external conditions, diminishes the capacity for sustained mental work, and leads to the development of structural changes in the connective tissues of the brain, spinal cord, and other organs. In infectious diseases and in cases of depression of the vital powers it is most useful as a restorative agent.

THE ENERGY OR HEAT VALUE OF THE FOOD PRINCIPLES

The food consumed not only restores the material metabolized and discharged from the body, but also the energy which has been expended as heat and mechanic motion. The food principles are products of the constructive processes taking place in the vegetable world during the period of growth and activity. At the time of their formation there is an absorption and storing of the sun's energy which then exists in a potential condition. During the metabolism of the animal body these compounds are reduced through oxidation to relatively simple bodies, such as carbon dioxid, water, urea, etc., with the liberation of their contained energy. All of the energy of the body, whatever its manifestations may be, can be traced to chemic changes going on in the tissues, and more particularly to those changes involved in the oxidation of the food principles.

It becomes, therefore, a matter of interest to determine the heat loss from the body in twenty-four hours for the purpose of subsequently determining if the energy contained in the foods, expressed in terms of heat, is present in amounts sufficient to compensate for the loss. The total quantity of heat liberated in the body and dissipated from it in twenty-four hours is determined by placing the subject in a respiration chamber provided with appliances containing water, by means of which the heat can be absorbed and measured. (See chapter on Animal Heat.) The unit of heat measurement is the Calorie, which is defined as the amount of heat necessary to raise the temperature of one kilogram of water 1°C. If therefore the volume of the water employed in the experiment expressed in kilograms be multiplied by the number of degrees of temperature through which it has been raised, the number of Calories will be known. The average number of Calories dissipated by a human being in various ways, *e.g.*, radiation, vaporization of water from lungs and skin, warming of foods, air, etc., has been estimated at from 2500 to 3000 each day. The question then to be determined is, whether any given diet scale contains this amount of energy and whether it can be liberated as heat on oxidation in the body.

The amount of heat or energy which any given food principle will yield can be determined by burning a definite amount (*e.g.*, 1 gram) to carbon dioxid and water and ascertaining the extent to which the heat thus liberated will raise the temperature of a given amount of water (*e.g.*, 1 kilogram). The amount of heat may be expressed in gram or kilogram degrees or calories, a gram calorie or kilogram Calorie being the amount of heat required to raise the temperature of a gram or a kilogram (1000 grams) of water 1° C. The apparatus employed for this purpose is termed a calorimeter, and consists essentially of a closed chamber in which the oxidation takes place, surrounded by a water jacket, the rise in temperature of the water indicating the amount of heat produced.

The results obtained by investigators employing different calorimeters and different food principles of the same group vary, though within certain limits: *e.g.*, 1 gram of casein yields 5.867 kilogram Calories; 1 gram of lean beef, 5.656 Calories; 1 gram of fat yields 9.353, 9.423, 9.686 Calories; 1 gram of carbohydrate, 4.182, 4.479, etc., Calories. These numbers represent the physical calorimetric heat values of these food principles.

In the human body as determined by calorimetric methods the oxidation of the food principles yields practically the same amount of heat they yield when oxidized outside the body, with the exception of the protein, which is oxidized only to the stage of urea. As this compound is capable of further reduction in the calorimeter to carbon dioxid and water with the liberation of heat, the quantity of heat it contains must therefore be deducted from the calorimetric heat value of the protein. According to Rubner, 1 gram of urea will yield 2.523 kilogram Calories. As the urea which results from the oxidation of 1 gram of protein is about $\frac{1}{3}$ of a gram, the amount of heat to be deducted from the heat value of the protein is $\frac{1}{3}$ of 2.523, or 0.841 Calories. It has also been shown that some of the ingested protein escapes in the feces, the heat value of which must also be determined and deducted. This having been done, the *physiologic* heat value becomes 4.124 Calories.

The following estimates give approximately the number of kilogram Calories produced when the food is burned to carbon dioxid, water, and urea in the body:

1 gram of protein yields	4.124 Calories.
1 gram of fat yields	9.353 Calories.
1 gram of carbohydrate yields	4.116 Calories.

The total number of kilogram Calories or kilogram degrees of heat yielded by any of the previously given diet scales can be readily determined by multiplying the quantities of food principles consumed by the above-mentioned factors. The diet scale of Vierordt, for example, yields the following:

120 grams of protein yields	494.88 Calories.
90 grams of fat yields	841.77 Calories.
330 grams of starch yields	1358.28 Calories.
	2694.93 Calories

The total Calories obtained from other diet scales would be as follows: Ranke, 2335; Voit, 3387; Moleschott, 2984; Atwater, 3331; Hultgren, 3436.

Starvation.—The relation of the different food principles to the general nutritive process becomes more apparent from an examination of the excretions from the body during the process of starvation combined with an examination of the organs and tissues after death. If an animal be deprived entirely of food, a decline in body-weight at once sets in, which continues until about 40 per cent. of the weight has been lost, when death generally ensues. This results from the fact that the active tissue cells consume, for the purpose of maintaining the normal temperature of the body, not only their own reserve food material, but that of the less active or storage tissues as well; and, in consequence, there is a progressive diminution in weight.

The phenomena which characterize this non-physiologic condition are as follows: hunger, intense thirst, gastric and intestinal uneasiness and pain, diminished pulse-rate and respiration, muscular weakness and emaciation, a lessening in the amount of urine and its constituents, diminished expiration of carbon dioxid, an exhalation of a fetid odor from the body, vertigo, stupor, delirium, at times convulsions, a sudden fall in body temperature, and finally death. The duration of life after complete deprivation of food varies from eight to thirteen days or more, though this period can be prolonged if the animal be supplied with water, this being more essential under the circumstances than the organic materials which can be supplied by the organism itself. The duration of the starvation period will naturally vary in accordance with the previous condition of the animal and the amount of reserve food, especially fat, the body contains.

The extent and the character of the metabolism that the body undergoes in starvation can be determined from an examination of the excretions. Thus the excretion of nitrogen declines very rapidly during the first few days —a fact which has been attributed to the consumption of the surplus protein food. The amount of nitrogen eliminated and hence the protein metabolized depend, mainly on the amount of protein consumed daily before the starvation period was inaugurated. At the end of four or five days when the surplus protein has been metabolized and the tissues begin to metabolize their own protein, the excretion remains fairly constant, from about 13 to 10 grams daily, until toward the close of the starvation period, when the amount eliminated falls very rapidly. In several instances of prolonged fasting by human beings the nitrogen elimination fell as low as 4 to 3.5 grams daily, indicating a protein metabolism only of from 25 to 18.75 grams. As proteins contain about 16 per cent. of nitrogen, 1 part of nitrogen equals

6.25 parts of protein. Hence, for every 1 gram of nitrogen or 2.14 grams urea excreted, it may be assumed that 6.25 grams of protein or, according to Voit, 30 grams of flesh have been metabolized. The daily excretion of urea, after the first five days therefore, indicates fairly accurately the extent of the metabolism of the tissue protein.

It has been observed also that there is a steady diminution in the excretion of carbon dioxid. As fat contains about 76 per cent. of carbon, 1 part of carbon equals 3.66 parts of carbon dioxid or 1.31 parts of fat. Hence, for every 1 gram of carbon or 3.66 grams carbon dioxid excreted it may be assumed that 1.31 grams of fat have been metabolized. The daily excretion of carbon, therefore, indicates the extent of fat metabolism. The carbohydrates are here left out of consideration, as they constitute only about 1 per cent. of the body-weight. It must be borne in mind, however, that in the metabolism of protein a certain quantity of fat or sugar is produced, which also undergoes oxidation. The amount of the carbon or the CO_2 that the protein would give rise to, as previously determined, must therefore be subtracted from that eliminated by the lungs, etc., in order to determine the amount of body-fat metabolized.

In a fasting experiment, voluntarily undergone by a human being, and lasting ten days, the metabolism of fat as shown by the CO_2 excreted amounted to 136.7 grams during the first four days and to 132 grams on the tenth day. In another similar experiment lasting five days, the fat metabolized amounted to 206 grams on the first day and 181 grams on the fifth day. As the starvation period lengthens the amount of fat metabolized gradually declines.

The following table shows the excretion of nitrogen and carbon and the calculated amounts of protein and fat metabolized from an experiment made by Ranke on himself during a fast of twenty hours, beginning twenty-four hours after the last meal:

Disintegration of Tissue (Calculated)			Expenditure (Determined)		
	Nitrogen	Carbon		Nitrogen	Carbon
Protein, 50 gm	7.8	26.5	Urea, 17 gm Uric acid, 0.2 gm	7.2	3.4
Fat, 199.6 gm	0.0	157.5	Carbon dioxid	0.0	180.6
	7.8	184.0		7.2	184.0

Coincidently with these losses to the body there is also a gradual loss of inorganic salts, and toward the termination of the period a sudden fall in temperature of several degrees centigrade, in consequence of the final consumption of all available foods, when death ensues. The immediate cause of death is not, however, apparent.

Post-mortem Appearances.—It has been experimentally determined that animals die when the body-weight has declined to about 40 per cent. Post-mortem examination shows that the loss of material, though very generally distributed throughout the body, is greatest in organs and tissues least essential to life.

The results of an analysis of the organs and tissues of a cat after a thirteen-day period of starvation, during which the animal lost 1017 grams in weight, are given in the following table, based on data furnished by Voit:

It will be observed from this table that the adipose tissue suffers the greatest loss, the entire amount disappearing with the exception of a small portion in the posterior part of the orbital cavity and around the kidneys. The muscles, though losing only 31 per cent. of their weight, yet furnish 429 grams of presumably protein material, for nutritive purposes. The heart and nervous system experience but slight loss.

Organ	Percentage Loss of weight	Actual Loss of Tissue
		Grams
Adipose tissue	97	267
Spleen	67	6
Liver	54	49
Testes	40	1
Muscles	31	429
Blood	27	37
Kidneys	26	7
Skin and hair	21	89
Lungs	18	3
Intestines	18	21
Pancreas	17	1
Bones	14	55
Heart	3	0
Nervous system	3	1

Mixed Diet.—The chemic composition of the tissues, taken in connection with their metabolism during starvation, implies that no one article of food is sufficient for tissue repair and heat production; but that all classes of foods—in other words, a mixed diet—are essential to the maintenance of a normal nutrition. Experimental investigation has also conclusively established this fact. Moreover, the amounts of nitrogen and carbon eliminated daily, and the ratio existing between them, indicate the amounts of protein, fat, and carbohydrate which are required to cover the loss.

Metabolism on a Purely Protein Diet.—Notwithstanding the chemic composition of the proteins and the possibility of their giving rise to either fat or a carbohydrate during their metabolism it has been found extremely difficult to maintain the normal nutrition for any length of time on a pure protein or fat-free flesh diet. This, however, has been accomplished with dogs. It was found, however, that, in order to maintain the nitrogen equilibrium, it was necessary to increase the proteins from two to three times the usual amount. Thus, a dog weighing 30 to 35 kilograms required from 1500 to 1800 grams of flesh daily in order to get the requisite amount of carbon to prevent consumption of its own adipose tissue. Under similar circumstances, a human being weighing 70 kilograms would require more than 2000 grams of lean beef—an amount which, from the nature of the digestive apparatus, it would be practically impossible to digest and assimilate for any length of time. Even the slight habitual excess beyond the amount normally required is imperfectly assimilated and gives rise to the production of nitrogen-holding compounds which, on account of the difficulty with which they are eliminated by the kidneys, accumulate within the body and develop the gouty diathesis, with all its protean manifestations.

Metabolism on a Fat and Carbohydrate Diet.—As nitrogen is an indispensable constituent of the tissues, it is evident that neither fat nor carbohydrates can maintain nutritive equilibrium except for very short periods. On such a diet the tissues consume their own proteins, as shown by the continuous excretion of urea, though the amount is less than during starvation. An excess of fat retards the metabolism of proteins. The same holds true for the carbohydrates.

Thus, in any well-arranged dietary there should be a combination of proteins, fats, and carbohydrates in amounts sufficient to maintain nutritive equilibrium; in other words, to repair the loss of tissue and to furnish the requisite amount of energy in accordance with work done, as well as with climatic and seasonal variations.

COMPOSITION OF FOODS

The food principles essential to the maintenance of the nutrition of the body are contained in varying proportions in compound substances termed foods; *e.g.*, meat, milk, wheat, potatoes, etc. Their nutritive value depends partly on the amounts of their contained food principles and partly on their digestibility. The dietary of civilized man embraces foods derived from both the animal and vegetable worlds.

The following tables show the percentage composition of the edible portions of foods as well as the amount of heat liberated per pound when oxidized in the body, according to Atwater and Bryant.

Composition of Animal Foods.—The following table shows the average percentage composition of various kinds of meats, cow's milk, and eggs:

Kind of Food Materials	Water	Unavailable Nutrients	Proteins	Fat	Carbohydrates	Ash	Fuel Value Per Lb. 453.6 Grams
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Calories
Beef:							
Loin, lean	67.0	1.2	19.1	12.1	....	1.0	900
Loin, fat	54.7	1.9	17.0	26.2	....	0.9	1470
Round, lean	70.0	1.0	20.7	7.5	....	1.1	735
Round, fat	60.4	1.6	18.9	18.5	....	1.0	1175
Veal:							
Cutlets (round)	70.7	1.3	19.7	7.3	....	0.8	710
Liver	73.0	0.9	9.7	5.0	....	1.0	410
Mutton:							
Leg	62.8	1.7	17.9	17.1	....	0.8	1095
Loin	50.2	2.4	15.5	31.4	....	0.6	1660
Pork:							
Loin chops	52.0	2.2	16.1	28.6	....	0.8	1555
Ham	53.9	2.1	14.8	27.5	....	0.6	1480
Fowl:	63.7	1.6	18.7	15.5	....	0.8	1040
Turkey	55.5	1.9	20.5	21.8	....	0.8	853
Mackerel	73.4	1.3	18.1	6.7	....	0.9	650
Halibut	75.4	1.1	18.0	4.9	....	0.8	570
Milk	87.0	0.5	3.2	3.8	5.0	0.5	310
Eggs, boiled	73.2	1.2	12.8	11.4	....	0.6	755

Meats.—It will be observed from these analyses that the meats contain from 18 to 20 per cent. of protein material. The proteins are two in number and are known as paramyosinogen or myosin and myosinogen or myogen, both of which are in a semi-fluid condition. The latter is four or five times as abundant as the former. After death these substances undergo coagulation and give rise to two solid substances known as myosin-fibrin and myogen-fibrin. After being subjected to the cooking process, meats contain the albuminoid body gelatin, a product of the transformation of the proteins of the connective tissue.

The percentage of fat contained within the meat substance is very small except in mutton and pork, where it rises to 5.4 per cent. and 5.8 per cent. respectively. The fat-globules in these meats are packed closely between the muscle-fibers, and prevent the easy entrance of the digestive fluids, and hence they are more difficult of digestion than beef. The large percentage of fat represented in the foregoing table is due to the presence in the food, as eaten, of adipose tissue which is an addition, not a constituent of meat.

The carbohydrates vary from 0.5 to 1 per cent., and are represented by glycogen. The principal inorganic salts are potassium phosphate and sodium chlorid.

The composition of meat will vary in composition in nutritive value and in energy-liberating capacity in accordance with the region of the body from which the specimen is taken.

Cooking, when properly done, not only makes the meat more palatable and appetizing from the development of agreeable flavors, but converts the connective tissue, which, in old animals especially, is tough and resisting, into gelatin, thus rendering it more easy of mastication and digestion. At the same time parasitic organisms, such as the embryonic forms of tenia or tapeworm, and *Trichina spiralis*, as well as bacterial growths, which frequently infest the bodies of animals, are destroyed and made harmless.

Milk is the natural food of the young of all mammals, and is usually regarded as typical on account of the ratio existing among its nutritive principles. The analysis given above is that of cow's milk. Examined microscopically, milk is seen to consist of a clear fluid, the milk plasma, holding in suspension an enormous number of small, highly refractive oil-globules, which measure on the average about $\frac{1}{10000}$ of an inch in diameter. Each globule is supposed by some observers to be surrounded by a thin albuminous envelope, which enables it to maintain the discrete form. Others deny the existence of such a membrane. The chief protein constituent of milk, caseinogen, is held in solution by the presence of phosphate of lime. On the addition of acetic acid or sodium chlorid up to the point of saturation the caseinogen is *precipitated* as such and may be collected by appropriate chemic methods. When taken into the stomach, caseinogen is *coagulated;* that is, it is changed into casein or tyrein. This change is brought about by the presence in the gastric juice of a special ferment termed rennin or pexin.

The fat of milk is more or less solid at ordinary temperatures. It is a combination of olein, palmitin, and stearin, with a small quantity of butyrin and caproin. When milk is allowed to stand for some time, the fat-globules rise to the surface and form a thick layer known as cream.

When subjected to the churning process, fat-globules run together and form a coherent mass—butter.

Lactose is the particular form of sugar found in milk. In the presence of *Bacillus acidi lactici*, the lactose is decomposed into lactic acid and carbon dioxid, the former of which not only imparts a sour taste to the milk, but causes a *precipitation* of the caseinogen. The chief salt found in milk is phosphate of lime, and this is the chief source of this agent in the formation of bones. Sodium and potassium chlorids are also present.

Eggs are also to be regarded as complete natural foods, inasmuch as they contain all the necessary food principles. The analysis given in the foregoing table represents the composition of the entire egg. The white of the egg contains 12 per cent. of protein and 2 per cent. of fat. The yolk, however, contains 15 per cent. of protein and 30 per cent. of fat.

Composition of Cereal Foods.—The average composition of the principal cereals is shown in the following table:

Kind of Food Material	Water	Unavailable Nutrients	Proteins	Fat	Carbohydrates	Ash	Fuel Value Per Pound 453.6 Grams
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Calories
Entire wheat flour	11.4	4.5	10.7	1.7	70.9	0.8	1645
Rye flour	12.9	3.6	5.3	0.8	76.9	0.5	1610
Rice	12.3	3.7	6.5	0.3	76.9	0.3	1610
Barley, pearled	11.5	4.0	6.6	1.0	76.10	0.8	1630
Buckwheat flour	13.6	3.5	5.2	1.1	75.9	0.7	1600
Corn meal	12.5	4.0	7.5	1.7	73.5	0.8	1625
Oat meal	7.8	5.6	13.4	6.6	65.2	1.4	1795
Whole wheat bread	38.4	3.2	7.5	0.8	49.1	1.0	1125
White bread	35.3	3.3	7.1	1.2	52.3	0.8	1195
Graham crackers	5.4	4.8	7.7	8.5	72.5	1.1	1900

That the cereals are most important and useful articles of diet is evident from their composition, consisting, as they do, of proteins and carbohydrates in large proportion. Owing to the cellulose or woody fiber which envelops and penetrates the grain, they are somewhat difficult of digestion. A section of a grain of wheat shows the external cellulose envelope, the husk, beneath which is a layer of large cells containing the chief protein—the gluten. The interior of the grain consists of small cavities, the walls of which are formed of cellulose and which contain the granules of starch, fat, small quantities of protein, and inorganic salts. All other cereals have a similar structure.

In the preparation of white flour from wheat it is customary to remove the husk, a process which involves the removal also of a portion, if not all, of the gluten cells, so that such flour contains less nitrogenized material than the original grain. It is possible, however, in the milling of wheat, to remove only the husk and retain the gluten in the flour, as in the preparation of whole wheat flour.

Bread is an artificially prepared food made either of wheat or rye. Owing to the fact that the proteins of the other cereals do not possess the same adhesive properties when kneaded with water, they cannot be used for bread-making purposes. In the making of bread, the flour is kneaded with water until a glutinous mass—dough—is formed. During this process, salt, sugar, and yeast are added. It is then kept in a temperature of about 100°F. In the presence of heat and moisture the natural ferment of the flour—diastase—converts a portion of the starch into sugar, which in turn is split up into carbon dioxid and alcohol by the yeast plant. The sugar that is added undergoes a similar change and hastens the process. The bubbles of carbon dioxid, becoming entangled in the dough, cause it to swell or rise and subsequently give the porous or spongy character to the bread. When baked at a temperature of 400°F., the alcohol is largely driven off; yeast cells and other organisms are destroyed; the starch, particularly that on the surface, is dextrinized. The principal salts contained in wheat flour are potassium and magnesium phosphate.

Composition of Vegetable Foods.—The average composition of some of the principal vegetables is shown in the following table:

Kind of Food Material	Water	Unavailable Nutrients	Proteins	Fat	Carbohydrates	Ash	Fuel Value Per Pound 453.6 Grams
	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Per cent.	Calories
Beans, lima, dried....	10.4	6.7	12.8	1.4	65.6	3.1	1565
Beans, lima, green....	68.5	2.7	5.3	0.6	21.6	1.3	525
Beans, white, dried...	12.6	7.5	15.8	1.6	59.9	2.6	1530
Beans, string, cooked[1]	95.3	0.5	0.6	1.0	1.9	0.7	90
Peas, dried..........	9.5	7.6	17.3	0.9	62.5	2.2	1508
Peas, green, cooked[1]..	73.8	2.5	5.1	3.1	14.4	1.1	490
Potatoes, boiled, cooked.[1]	75.5	1.7	1.9	0.1	20.0	0.8	415
Potatoes, sweet.......	51.9	3.0	2.2	1.9	40.3	0.7	885
Beets, cooked[1].......	88.6	1.2	1.7	0.1	7.2	1.2	170
Cabbage............	91.5	0.7	1.2	0.3	5.5	0.8	140
Tomatoes...........	94.3	0.4	0.7	0.4	3.8	0.4	100
Turnips.............	89.6	0.8	1.0	0.2	7.8	0.6	175
Egg-plant..........	92.9	0.6	0.9	0.3	4.9	0.4	120
Spinach, fresh.......	92.3	1.0	1.6	0.3	3.2	1.6	100
Asparagus, cooked. ..	91.6	1.0	1.7	3.0	2.1	0.6	195

The vegetable foods, as a class, vary considerably in nutritive value and digestibility, the latter depending on the amount of cellulose they contain. A section of a vegetable shows not only the presence of an external cellulose envelope, but also an inner framework which penetrates its substance in all directions. The nutritive principles are contained in small cavities, the walls of which are formed by the framework. Nearly all vegetables require cooking before being eaten. When subjected to heat and moisture, not only is the texture of the vegetable softened and disintegrated, but the starch grains are hydrated and partially prepared for conversion into dextrin and sugar. At the same time various savory substances are set free, which make the food more palatable.

Beans and **peas** contain large quantities of a protein, legumin, and starch, and hence are especially valuable as nutritive foods. The presence of the cellulose envelope, especially in ripe beans and peas, combined with rather a dense texture, renders them somewhat difficult of digestion. **Potatoes,** though largely employed as food, are extremely poor in protein, 2 per cent., and carbohydrates, 20 per cent. When sufficiently cooked they are easily digested, owing to the small amount of cellulose they contain.

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[1] With butter etc., added.

Green vegetables, *e.g.*, lettuce, spinach, tomatoes, asparagus, onions, etc., though containing food principles in small amounts, are, nevertheless, valuable adjuncts to the dietary, for the reason that they contain inorganic as well as organic salts, which appear to be necessary to the maintenance of the normal nutrition. The want of green vegetables has been supposed to be the cause of scurvy.

Ripe fruits, grapes, cherries, apples, pears, peaches, strawberries, lemons, oranges, etc., though consumed largely, possess but little nutritive value. They consist largely of water, 75 to 85 per cent., proteins a trace, sugar from 5 to 13 per cent., organic acids (citric, malic, tartaric), pectose, and various inorganic salts.

Relative Value of Animal and Vegetable Foods.—Though both animal and vegetable foods contain the different classes of food principles, it is not a matter of entire indifference as to which are consumed. It has been found by experiment that animal proteins are more easily and completely digested and absorbed than vegetable proteins; that cellulose is not only highly indigestible, but by its presence in large quantities retards the digestive process and impairs the activity of the entire digestive mechanism, though in moderate quantity it undoubtedly aids digestion indirectly by mechanically promoting peristalsis. The following table shows the relative digestibility and availibility of the two classes of foods:

Weight of Food	Vegetable		Animal	
	Digested	Undigested	Digested	Undigested
Of 100 parts of protein........	84.00	16.00	97	3
Of 100 parts of fat	90.00	10.00	95	5
Of 100 parts of carbohydrate.........	97.00	3.00	98	2

CHAPTER X

DIGESTION

Digestion is a process partly physical, partly chemic, by which the nutritive principles of the foods are prepared for absorption. The reason for these changes lies in the fact that the foods as consumed are heterogeneous compounds consisting of organic and inorganic nutritive principles associated with a varying amount of non-nutritive material, such as the dense parts of the connective tissue of the animal foods and the woody fiber or cellulose of the vegetable foods, from which the nutritive principles must be freed before they can be utilized; and in the further fact, that even when consumed in the free state, the food principles are seldom in a condition to be absorbed into the blood and subsequently assimilated by the tissues. When foods are consumed in their natural state or after they have been subjected to the cooking process, they are subjected while in the food canal to the solvent action of various fluids by which they are disintegrated and reduced to the liquid condition. The nutritive principles freed from their combinations are changed in chemic composition and transformed into substances capable of absorption. To all the physical and chemic changes which foods undergo in the food canal the term digestion has been given.

The Digestive Apparatus.—The digestive apparatus comprises the entire alimentary or food canal and its various appendages: the lips, the teeth, the tongue, the salivary glands, the gastric and intestinal glands, the pancreas, and the liver (Fig. 60).

The alimentary canal is a musculo-membranous tube about eleven meters in length, and extends from the mouth to the anus. It may be subdivided into several distinct portions, as mouth, pharynx, esophagus, stomach, small and large intestines. The mouth is provided (1) with teeth, by which the food is divided, (2) with the tongue, and (3) with glands, by which a solvent fluid, the saliva, is secreted. The glands, though situated for the most part outside the mouth, are connected with it by means of ducts. Posteriorly the mouth opens into the pharynx or throat, a somewhat pyramidal-shaped structure about twelve centimeters in length, which in turn is followed by the esophagus or gullet, a tube about twenty-two centimeters in length. As the esophagus passes through the diaphragm it expands into the stomach, a curved pyriform organ, which serves as a reservoir for the reception and retention of the food for a varying length of time. The small intestine is that portion of the alimentary canal extending from the end of the stomach to the beginning of the large intestine in the right iliac fossa; owing to its length, about eight meters, it presents a very convoluted appearance in the abdominal cavity. Embedded in its walls are the intestinal glands which open on its surface and secrete the intestinal fluid. In the upper portion of the small intestine, within twelve centimeters of the stomach, there is an orifice, the outlet of a small pouch, the Ampulla of Vater, into which open the terminations of the ducts of the liver and pancreas, organs which secrete the bile and pancreatic juice respectively. The large intestine is from one and three quarters to two meters in length and extends from the end of the small intestine to the anus. Its walls contain a large number of glands.

The general process of digestion is largely accomplished by the chemic action of the digestive fluids secreted by glands, some of which are imbedded in the walls of the canal while others are situated outside of it and communicate with it only by means of ducts. These fluids are the saliva, the gastric, intestinal, and pancreatic juices, and the bile. Though taking place throughout a large portion of the food canal, the process may be subdivided into several stages: viz., prehension, mouth digestion, deglutition, gastric digestion, and intestinal digestion.

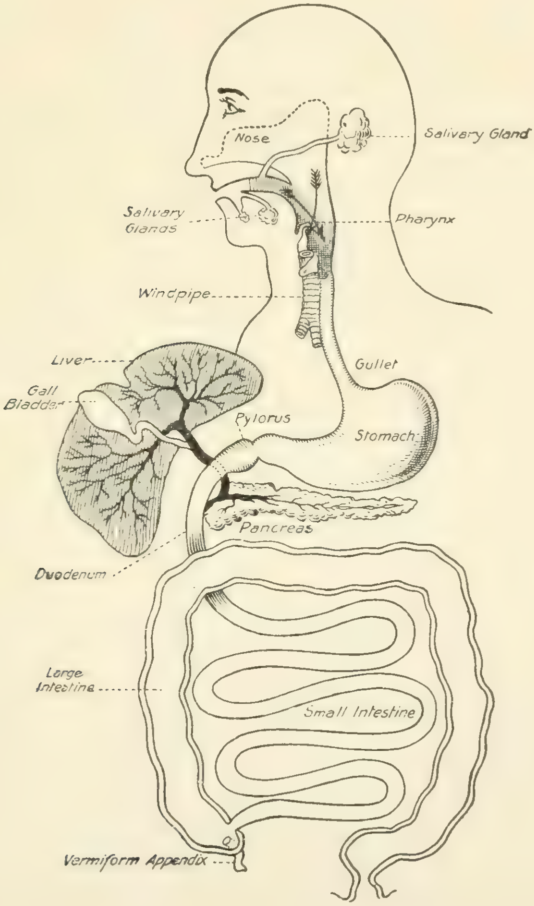
Nose
Salivary Gland
Salivary Glands
Pharynx
Windpipe
Liver
Gall Bladder
Gullet
Pylorus
Stomach
Pancreas
Duodenum
Large Intestine
Small Intestine
Vermiform Appendix

Fig. 61.—Diagram of the Alimentary Canal.—(*Modified from Landois.*)

As a result of the action of these fluids the nutritive principles are prepared for absorption into the blood; the non-nutritive principles, along with certain waste products, pass into the large intestine to be finally extruded from the body.

FERMENTS; ENZYMES

In a preceding chapter it was stated that under favorable conditions the carbohydrates, fats, and proteins undergo reduction to simpler compounds as a result of the action of agents such as the yeast plant and various forms of bacteria. To this process of reduction the term fermentation, and to the agent which causes the fermentation the term ferment, or enzyme has been given. As these compounds undergo reduction to simpler substances somewhat different in character in the alimentary canal during the period of digestion as a result of the action of ferments, it will be conducive to clearness of ideas regarding the nature of the digestive process if the nature and properties of ferments in general are briefly considered at this time.

A ferment or an enzyme may be defined as an agent that induces a change of state, or a change in composition of an organic compound, for the most part hydrolytic, without itself being utilized in the process or appearing in the end-results of the process.

Ferments have been divided for a long time into two classes, *viz.*, organized and unorganized. Among the organized ferments may be mentioned the yeast plant (*Saccharomycetes*) and various forms of bacteria; among the unorganized ferments may be mentioned the diastase that transforms the starch of barley, wheat, or other cereals into sugar, as well as ptyalin, pepsin, steapsin or lipase, and other ferments contained in the digestive fluids that transform or reduce the food principles to simpler compounds.

It will be recalled that if the yeast plant is added to a sugar solution containing in addition some protein and various inorganic salts such as phosphates and the solution kept at a favorable temperature the yeast cells soon begin to grow and multiply. Coincidently the sugar is reduced for the most part to carbon dioxid and alcohol. The carbon dioxid bubbling through the solution as steam bubbles through water that is boiling, gave rise to the expression fermentation (from *fervere*, to boil), and as this was attributed to the life activities of the yeast plant it was called a ferment.

Again, if dead protein matter is exposed to air and moisture at a suitable temperature it will be invaded by various species of bacteria, which in a short time will begin to grow and multiply. Coincidently the protein molecules are reduced to simpler compounds, such as hydrogen sulphid, ammonia, carbon dioxid and a number of other compounds, the nature of which will vary with the character of the protein. As this reduction is accompanied by the bubbling of gases through the surrounding liquid, it too has received the name of fermentation, and as the reduction is attributed to the life activities of the bacteria they too have been called ferments. In both instances the ferment is a unicellular plant possessing a distinct organization. For this reason they have been termed *organized* ferments.

When grains of barley or other cereals containing starch are exposed to moisture and a suitable temperature, the starch is gradually changed to sugar, a transformation attributed to the action of a ferment. When the starches, fats, proteins, and compound sugars are introduced into the alimentary canal they are also reduced to simpler compounds, a reduction attributed to the action of a series of distinct and specific ferments. In addition to the changes that the food principles undergo in the alimentary canal, the corresponding principles as well as many other compounds undergo similar changes in the body tissues as the result of the action of ferments, changes that underlie and condition many if not all the phenomena of the nutritive process. In none of these instances, however, has the ferment been satisfactorily isolated or its chemic or physical features determined. For this reason these ferments have been termed *unorganized* ferments. Investigations have demonstrated, however, that they are products of the metabolism of the cells of plant and animal tissues.

In recent years the distinction between organized and unorganized ferments has become untenable owing to the fact that chemists have succeeded in extracting from yeast cells as well as from bacterial cells, enzymes or ferments that produce in sugar and protein the same reduction effects under the same conditions as in the case of yeast cells and bacteria themselves. It is therefore probable that these organized cells act not directly by virtue of their own activities, but indirectly, by virtue of an unorganized ferment which they secrete and discharge into the surrounding medium. All enzymes that produce their effects after being discharged from cells are termed *extra-cellular* enzymes, while those that produce their effects in the interior of cells are termed *intra-cellular* enzymes.

The Nature of Enzymes.—An enzyme is in all probability organic in character, though neither its chemic nature nor composition has been determined. Some of them exhibit protein, others carbohydrate reactions, but by reason of the difficulty in isolating enzymes and of freeing them absolutely from all traces of protein and carbohydrates it is not possible to state positively whether the reactions observed are due to the enzyme or its associated organic matter. The purer the preparation, however, the less of any chemic reaction is exhibited.

From what is known of their action, of the effects produced and of the conditions under which they act, ferments have a resemblance to various inorganic substances or agents that produce changes of composition and decomposition apparently by their presence alone, for, as far as the evidence goes, they neither enter into the end-products of the reaction nor are they destroyed. A chemic change thus produced is termed *catalysis* and the agent causing it is termed a *catalyzer* or *catalyst.* The substance on which the catalyst acts is termed the *substrate.* In most, if not in all instances a catalyst acts not as an initiator, but as an accelerator of a change that would spontaneously take place with extreme slowness and in some instances with results so slight as to be inappreciable. Oxygen and hydrogen, for example, spontaneously combine, there are reasons for believing, at room temperatures though at such a slow rate that the formation of water cannot be detected, but if a small quantity of finely divided platinum be added the combination takes place almost immediately; carburetted hydrogen and oxygen combine when they pass over platinum with the formation of carbon dioxid and water; saccharose and water in the presence of hydrochloric acid will combine and be reduced to equal quantities of levulose and dextrose; dilute peroxid of hydrogen will slowly decompose spontaneously and yield up oxygen, but if finely divided platinum or silver be added the decomposition is greatly accelerated. In all these instances, to which many more might be added, the catalyst, simply by its presence accelerates a change spontaneously taking place without itself appearing in the end-products of the reaction.

It has been experimentally demonstrated that the finer the catalyst is divided or the greater the surface it presents the more energetically it acts. Thus, if platinum, silver, or gold be changed to the colloidal state,[1] a state in which the particles of ultramicroscopic size are held in solution or perhaps suspension they become extremely active catalyzers even in exceedingly small quantities.

From the foregoing facts and from many others it may be assumed that the unorganized enzymes exist in the colloidal state.

The Rate and Completeness of Enzymic Action.—The rate and completeness of enzymic action are influenced by a variety of conditions, among the more important of which are temperature and the rapidity of the removal of the products of their action.

Temperature.—All enzymes are sensitive to changes in temperature. At 0°C. they appear to be incapable of inducing changes in organic matter. As the temperature is raised their reaction properties develop and increase in velocity, until a temperature of 40°C. to 50°C. is reached, when they are at their maximum. For this reason this degree of temperature is spoken of as the *optimum* temperature. Beyond 50°C. the velocity of their action begins to decrease and at 60°C. it comes to an end for the majority of enzymes. At 100°C. all reaction ceases for the reason that the enzymes are destroyed, especially if they are moist.

The Removal of the Products of Enzymic Action.—The completeness of enzymic action will depend on the rapidity with which the products of enzyme activity are removed. This is illustrated in the following: If a substrate such as fat and the enzyme lipase be mixed with water in a dialyzing test-tube, the fat will combine with water, after which the fat will undergo a cleavage into a fat acid and glycerin. If the products of the reaction are removed practically as rapidly as they are formed the reaction will continue until all the fat is so transformed. Under such circumstances the action will be complete. If, however, the reaction takes place in a receptacle the character of which prevents the removal of the fat acid and glycerin, the reaction will in time come to an end, leaving apparently a percentage of fat unchanged. The explanation at one time given for the cessation of the reaction was that the accumulation of the products interfered with the further action of the enzyme. It is, however, now generally admitted that under the circumstances the ferment, shortly after the appearance of the cleavage products, initiates a reverse action, *i.e.*, recombines the fat acid and glycerin with the re-formation of the fat until a condition of chemic equilibrium is established between the opposing tendencies. The discovery that many ferments are thus capable of secondarily reversing their primary action has assisted in the interpretation of a number of obscure physiologic processes. It must not be overlooked that in this instance the enzyme does not initiate the reverse action, but merely hastens what would take place by reason of a want of chemic equilibrium between the substances present.[2]

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[1] The colloidal state may be developed by passing an electric current through electrodes of these metals placed in distilled water. With the passage of the current particles of the metals are discharged from one of the electrodes into the water in the form of a cloud.

[2] Reversibility of a chemic reaction may be defined as a recombination of the products of the reaction of the original compound until a condition of equilibrium is established between the analytic and the synthetic tendencies. A classic illustration of the two phases of a chemic reaction is the following: If chemically equivalent amounts of acetic acid and ethyl alcohol are mixed at a definite temperature a reaction occurs which eventuates in the formation of ethyl acetate and

The Specific Action of Enzymes.—The number of enzymes in the digestive fluids and in the various tissues of the body has given rise to the idea, which has been confirmed by experiment, that an enzyme exerts its action on but one substrate, in other words, that its action is specific. Thus an enzyme that would transform starch into sugar would not be capable of causing a cleavage of fat into a fat acid and glycerin; an enzyme that would cause a cleavage of saccharose would not be capable of causing a cleavage of lactose. So with all other enzymes. Each seems to be specially adapted to catalyze but one substrate under given conditions. Various other features of enzymes, their mode of action, their origin from preëxisting substances, the methods by which they are made active, the conditions under which they are most active, etc., will be mentioned in connection with a consideration of the fluids and tissues in which they are present.

MOUTH DIGESTION

The digestion of the food as it takes place in the mouth comprises a series of physical and chemic changes, the result of the action of the teeth, the tongue, and the saliva. The mechanic division of the food and the incorporation of the saliva with it are termed respectively mastication and insalivation.

MASTICATION

Mastication is the mechanic division of the food, and is accomplished by the teeth and the movements of the lower jaw under the influence of muscle contractions. Complete mechanic disintegration of the food is important for its subsequent solution and chemic transformation; for when finely divided it presents a larger surface to the action of the digestive fluids and thus enables them to exert their respective actions more effectively and in a shorter period of time.

The Teeth.—In man passing from childhood to adult life two sets of teeth make their appearance. The first set constitute the temporary, deciduous, or milk teeth; the second set constitute the permanent teeth, which should last with proper care through life or to an advanced age.

The temporary teeth, twenty in number, ten in each jaw, though smaller than the permanent teeth, have the same general conformation. They are divided into four incisors, two cuspids or canines, and four molars for each jaw.

The permanent teeth, thirty-two in number, sixteen in each jaw, are divided into four incisors, two cuspids or canines, four bicuspids or premolars, and six molars for each jaw.

Each tooth may be said to consist of three portions: (1) the crown,

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water. In this instance after a certain percentage of these substances has thus united the products of the reaction begin to recombine with the formation of the original compounds until the opposing tendencies are in equilibrium, a state in which they remain so long as the conditions remain unchanged. Again, if maltose and water be mixed, a reaction occurs which eventuates in the formation of dextrose. In time the dextrose molecules combine to form maltose and water until a condition of equilibrium is established. If the yeast enzyme be added the reactions both analytic and synthetic are increased in velocity. The enzyme, however, does not initiate, but merely hastens a reaction already taking place.

or that portion which projects above the gums; (2) the root or fang, that portion embedded in the alveolar socket; (3) the constricted portion or neck, which is surrounded by the free margin of the gum. The teeth are firmly secured in their sockets by a fibrous membrane, the peridental membrane, which is attached, on the one hand, to the alveolar process, and, on the other, to the cementum.

A vertical section of a tooth shows that it consists of three distinct solid structures, the enamel, the dentine, and the cementum, which have the anatomic relationship represented in Fig. 62. In the center of the dentine there is a cavity the general shape of which varies in different teeth, and which is occupied during the living condition by the tooth pulp.

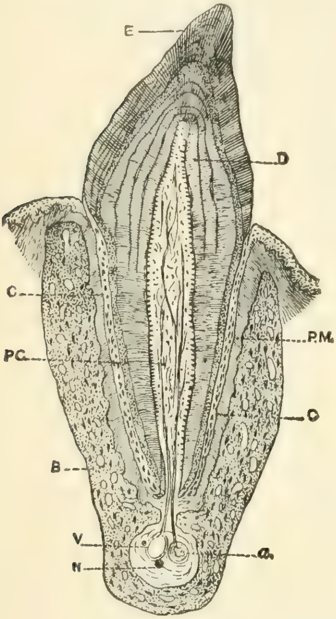

Fig. 62.—Vertical Section of Tooth in Jaw. *E.* Enamel. *D.* Dentine. P. M. Periodontal membrane. *P.C.* Pulp cavity. *C.* Cement. *B.* Bone of lower jaw. *V.* Vein. *a.* Artery. *N.* Nerve.—(*Stirling.*)

Microscopic examination of the tooth reveals the presence of irregular stellate spaces, the interglobular spaces, between the dentine and the cementum, which are occupied by connective-tissue cells. Clefts of varying size are also observed at the junction of the dentine and the enamel, and extending for some distance into the latter.

The *enamel* is composed of dense hard cylinders which, on account of their small size and close relationship, appear to be hexagonal in shape. These cylinders are held together by cement substance. The free border of the enamel is covered by a thin membrane known as the cuticle or membrane of Nasmyth.

The *dentine* is somewhat less dense than the enamel. It is composed of connective-tissue fibers embedded in a ground-substance, both of which have undergone calcification in the course of development. The dentine is penetrated by a series of fine canals, the dentine canals or tubules, which begin by open mouths on the pulp side. From this point the tubules pass outward to the cementum and enamel, where their terminal branches communicate with and terminate in the interglobular spaces and clefts. In their course the tubules give off a series of branches which communicate freely with one another. The dentine bordering the tubule is somewhat more dense than the intertubular portion and constitutes what is known as the dentinal sheath or Neumann's sheath.

The *cementum* resembles bone because it contains both lacunæ and canaliculi, though it is, as a rule, devoid of Haversian canals.

The *pulp* consists of a framework of connective tissue which affords support for blood-vessels and nerves, both of which enter the pulp chamber through a small foramen at the apex of the root. The outer surface of the pulp is covered with a layer of large spheric cells, the odontoblasts.

Each cell presents on its inner surface short processes which pass into the pulp; on its outer surface it presents a long process which enters a dentine tubule and extends as far as its ultimate terminations. Collectively these processes are known as the dentine fibers. Inasmuch as the fibers do not completely occupy the lumen of the tubule, it is probable that there is a free circulation of lymph from the pulp chamber through the dentine tubules into the enamel clefts, into the interglobular spaces, and possibly into the lacunæ of the cementum.

The *peridental membrane* is composed of connective-tissue fibers abundantly supplied with blood-vessels and nerves.

Movements of the Lower Jaw.—The lower jaw is capable of a downward and upward, an antero-posterior, and a lateral movement, all dependent on the peculiar construction of the joint.

Temporo-maxillary Articulation.—This articulation is formed by the anterior portion of the glenoid cavity, the eminentia articularis, and the condyle of the inferior maxilla, all of which are united by means of ligaments. Situated between the glenoid cavity and the condyle is a plate of fibro-cartilage oval in shape and biconcave. This cartilage divides the joint into two cavities—one above, the other below—each of which is provided with a synovial membrane. The function of the cartilage is to present constantly an articulating surface to the condyle in the various movements of the lower jaw, which it is enabled to do by virtue of its mobility.

In the downward movement of the lower jaw each condyle glides forward, carrying with it the interarticular fibro-cartilage, the upper concave surface of which is applied to the convex surface of the eminentia articularis. In the upward movement of the jaw both the condyles and the cartilages pass backward and resume their normal position. The movements of depression and elevation are made possible by the slightly oblique direction of the condyle. In the carnivorous animals, whose food requires considerable cutting, these movements are especially well developed. In these animals the condyles are transversely arranged and at right angles to the long axis of the jaw. In the antero-posterior movement the jaw moves in a horizontal direction and the condyles and the articular cartilages glide forward and backward in the glenoid fossæ. In the rodent animals the long axis of the condyle runs in the antero-posterior direction, which allows of a considerable gliding movement. When the jaw performs a lateral movement, the condyle and cartilage of one side may remain in their natural position while the opposite condyle and cartilage glide forward in the glenoid fossa, directing the symphysis of the jaw to the opposite side of the median line. The lateral movements are well exhibited by the herbivorous animals, in which they are quite extensive, and made possible by the small size of the condyle and the large extent of articulating surface. In man the structure of the joint is such as to admit of all these possibilities, and the lower jaw acquires in consequence great freedom of movement.

The Functions of the Muscles of Mastication.—The movements of the lower jaw are caused by the action of numerous muscles, which, having fixed points of origin, are attached to various points on its surface. The muscles concerned in the movements of mastication are presented in the following table:

Anterior belly of digastric Mylohyoid Geniohyoid	Depress the lower jaw and open the mouth.
Temporal Internal portion of masseter Internal pterygoids	Elevate the lower jaw and close the mouth.
External pterygoids External portion of masseter Anterior fibers of temporal	Draw the lower jaw forward and cause the lower teeth to project beyond the upper.
Posterior fibers of temporal Internal portion of masseter Digastric, mylohyoid, and geniohyoid	Draw the lower jaw back to its normal position.
Internal pterygoids External pterygoids	Contracting alternately, draw the jaw to the opposite side.
Pterygoids, external and internal Temporal Masseter	Produce grinding movements of the lower jaw.

The action of the depressor muscles becomes apparent when their points of origin and insertion are considered. The anterior belly of the digastric, the mylohyoid, and the geniohyoid muscles, agree in having a similarity of origin—the hyoid bone—and a common area of insertion, the anterior portion of the lower jaw. Their anatomic relation is such that their combined action will depress the lower jaw and open the mouth.

The action of the elevator muscles becomes apparent when their points of origin and insertion are considered. The elevator muscles arise from various points on the side of the head, and are inserted into the coronoid process, ramus, and internal surface of the angle of the lower jaw. After the mouth has been opened, the simultaneous contraction of these muscles will elevate the jaw and closes the mouth with considerable force. The power of these muscles, which is very great, depends on the shortness and thickness of the muscle-bundles.

The action of the rotator muscles, the external and internal pterygoids, those which give rise to the lateral movements of the jaw, depends in like manner on their origin and insertion. The first arises from the outer surface of the external pterygoid plate and the great wing of the sphenoid bone; the second arises mainly from the inner surface of the external pterygoid plate; they are inserted into the neck of the condyle and angle of the lower jaw respectively. When they contract, the condyle on the corresponding side is drawn forward, while the opposite condyle remains stationary. As a result, the symphysis of the jaw is directed to the opposite side. The grinding movements of the jaw are produced by the coördinated action of all the groups of muscles acting more or less successively.

For the proper mastication of the food it is essential that it be kept between the opposing surfaces of the teeth. This is accomplished by the contraction of the orbicularis oris and buccinator muscles from without and the tongue muscles from within.

The Nerve Mechanism[1] of Mastication.—Mastication is a complex act and involves the coöperation of a number of muscles, afferent and efferent nerves, and a central mechanism by which they are excited to, and coördinated in their activity. The central mechanism is located in the medulla oblongata in the gray matter beneath the floor of the fourth ventricle.

During the intervals of mouth digestion the mouth is closed by the contraction of the elevator muscles of the lower jaw. When the occasion arises for the introduction of food, the mouth is opened by the depressor muscles; after the food is introduced into the mouth it is again closed and that combination of muscle contractions initiated which when continued results in the mechanical division of the food.

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[1] By this term is meant a combination of nerves, afferent and efferent, and nerve centers which when excited to action coördinates the actions of the organs with which it is associated.

The nerves and nerve centers constituting the nerve mechanism for mastication are shown in the following table:

Afferent Nerves.	Nerve-center.	Efferent Nerves.
1. Lingual and buccal branches of the trigeminal nerve.	Medulla oblongata.	1. Small root of the trigeminal nerve.
2. Glosso-pharyngeal.		2. Hypoglossal.
		3. Facial or portio dura.

The Efferent Nerves.—The efferent nerves that transmit nerve impulses to the various muscles of mastication are the small root of the trigeminal, the hypoglossal, and the facial.

The *small root* of the *trigeminal nerve* after emerging from the cavity of the cranium through the foramen ovale joins the inferior maxillary division of the large sensor root. After a short course the efferent fibers separate into two groups, an upper and a lower; the upper group is distributed to the masseter, temporal, internal and external pterygoid muscles, the lower group is distributed to the mylohyoid and anterior belly of the digastric muscles. The *hypoglossal* nerve, after emerging from the cranium through the anterior condyloid foramen, passes downward and forward to be distributed to the intrinsic and extrinsic muscles of the tongue. The *facial* or *portio dura* after emerging from the stylo-mastoid foramen is distributed to the superficial muscles of the face.

Stimulation of any one of these nerves with induced electric currents gives rise to convulsive movements in the muscles to which it is distributed while its division is followed by paralysis of the muscles.

The Central Mechanism.—The central mechanism that excites and coördinates the action of the nerve-cells from which these nerves emerge, may be excited to activity (1) by nerve impulses descending from the cerebrum as a result of volitional efforts; and (2) by nerve impulses transmitted through afferent nerves from the mouth. Though movements of mastication are primarily volitional and may so continue, nevertheless when once initiated they continue for an indefinite period, so long in fact as the nerve impulses which the food develops in afferent nerves are received by the central mechanism, thus falling into the category of secondary or acquired reflex acts. That the masticatory movements are of this reflex character is indicated by the fact that they will be maintained, even though the volitional effort that called them forth has subsided and the attention has been directed to some entirely different subject. It would appear that all that is necessary under such circumstances is the stimulating action of the food upon the peripheral terminations of the afferent nerves distributed to the mucous membrane of the tongue and mouth.

The Afferent Nerves.—The afferent nerves, stimulation of which excites the central mechanism, are the lingual and buccal branches of the *superior* and *inferior maxillary* divisions of the *trigeminal nerve*, the lingual branches of the *glosso-pharyngeal*, and in all probability the gustatory fibers of the *chorda tympani*. The introduction of food into the mouth develops in the peripheral terminations of these nerves, by reason of its physical and chemic properties, nerve impulses which are then transmitted to the central mechanism. If these nerves are divided, mastication is seriously impaired. When divided and their central ends stimulated with induced electric currents, the muscle will reflexly be thrown into contraction.

INSALIVATION

Insalivation is the incorporation of the saliva with the food, and takes place for the most part during mastication. The saliva ordinarily present in the mouth is a complex fluid composed of the secretions of the parotid, submaxillary, and sublingual glands and the muciparous follicles of the mouth, which collectively constitute the salivary apparatus.

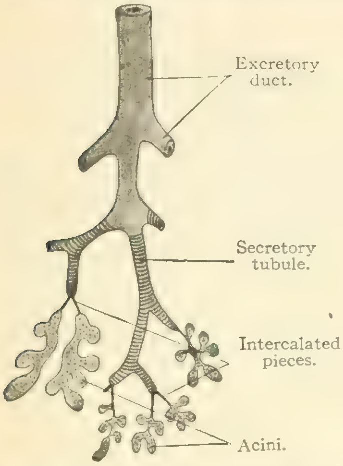

FIG. 63.—SCHEME OF THE HUMAN SUBMAXILLARY GLAND.—(*Stöhr.*)

The **parotid gland** is situated in front of and partly below the external ear, where it is held in position by the fascia and skin. From the anterior border of the gland there emerges a duct (Stenson's), which, after crossing the masseter muscle to its anterior border, turns inward, pierces the buccinator muscle and opens on the surface of the cheek opposite the second upper molar tooth.

The **submaxillary gland** is situated below the jaw in the anterior part of the submaxillary triangle. From the gland there emerges a duct (Wharton's) which opens into the mouth by a minute orifice on the surface of a papilla by the side of the tongue.

The **sublingual gland** is situated just beneath the mucous membrane in the anterior part of the mouth, where it forms a projection between the gums and tongue. The posterior part of the gland gives origin to a duct (the duct of Rivinus, described also by Bartholin) which opens into the mouth with or very near to the duct of Wharton. The anterior part of the gland gives origin to a varying number of ducts (the ducts of Walther) which open separately along the edge of the sublingual plica of the mucous membrane.

Histologic Structure of the Salivary Glands.—In their ultimate structure the salivary glands bear a close resemblance to one another. They are compound tubulo-alveolar glands composed of small irregularly shaped lobules united by areolar tissue, and connected by branches of the salivary ducts. Each lobule is made up of a number of small alveoli or acini more or less tubular in shape which are the terminal expansions of the smallest ducts. (See Fig. 63.) The wall of the acinus is formed by a reticulated basement membrane, surrounded externally by blood-vessels, the spaces between which constitute lymph-spaces or channels. The inner surface of the acinus membrane supports a single layer of irregular spheric or polygonal epithelial cells. The cells do not entirely fill up the cavity of the acinus, but leave an intercellular space, the lumen, which constitutes the beginning of the duct for the transmission of the secretion to the mouth. From each acinus there passes a narrow intercalary duct lined by a layer of flattened cells. The common excretory duct—formed by the union of the intralobular and interlobular ducts—consists also of a basement membrane, lined, however, by tall columnar epithelial cells. The salivary glands are abundantly supplied with blood-vessels and nerves which are closely related to their activity.

Based partly on the character of their secretions and partly on the microscopic appearance of their secreting cells, the salivary glands have been divided by Heidenhain into two classes: viz., serous or albuminous, and mucous glands. To the first class belong the parotid, a portion of the submaxillary, and a portion of the glands of the tongue. To the second class belong a portion of the submaxillary gland, the sublingual, a portion of the glands of the tongue, the glands of the cheeks, lips, palate, and pharynx. It is possible that a single alveolus of any gland may contain both albuminous and mucous cells.

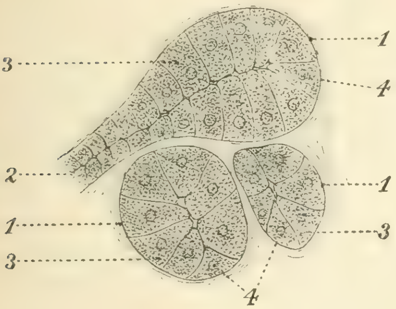

FIG. 64.—PAROTID GLAND AT REST. 1,1, Acini; 2, duct; 3,3, albuminous cells filled with fine granules; 4,4, nuclei almost concealed. (Semi-diagrammatic.)

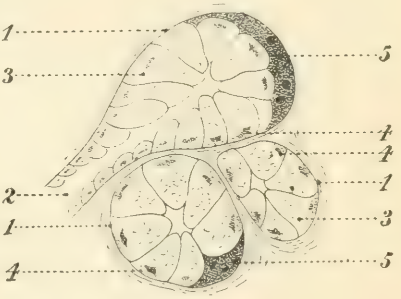

FIG. 65.—SUBMAXILLARY GLAND AT REST. 1,1, Acini; 2, duct; 3, 3, mucous cells containing mucin; 4,4, nuclei, flattened and dispersed toward the base of the cells; 5,5, crescents of Giannuzzi.—(*After Vialleton.*)

In the *serous* glands the cells are more or less spheric in shape, nucleated, and almost completely filled with dark granular material (Fig. 64). In the *mucous* glands the cells are large, clear in appearance, and loaded with a highly refracting material resembling mucin (Fig. 65). Between the basement membrane and the clear cells are to be found in the acini of the submaxillary glands small crescentic shaped cells filled with granular material which stains deeply with various coloring matters. These are known as the demilunes of Heidenhain. At one time it was supposed that they were young cells destined to take the place of the clear cells which were believed to be exhausted and to have undergone disintegration. At the present time they are regarded as albuminous or serous cells which exhibit changes similar to the cells of the parotid gland.

The glands embedded in the mucous membrane covering the tongue, lips, cheek, palate, and pharynx are for the most part lined with epithelial cells which contain a highly refracting matter similar to, if not identical with, that found in the cells of the submaxillary and sublingual glands.

Nerve-supply.—Histologic investigation has demonstrated that the cells and blood-vessels of the salivary glands are supplied with nerve-fibers directly from ganglion cells situated in their immediate neighborhood. Thus the cells and blood-vessels of the submaxillary and sublingual glands, receive nerve-fibers from the submaxillary, sublingual and superior cervical ganglia, while the cells and blood-vessels of the parotid gland receive nerve-fibers from the otic and the superior cervical ganglia. From their ultimate distribution it may be inferred that some of the ganglion cells and fibers influence the production of the secretions (secretor nerves), while others influence the caliber of the blood-vessels causing either constriction or dilatation (vaso-constrictor and vaso-dilatator nerves). (Fig. 68.) The secretor fibers penetrate the basement membrane enclosing the gland acinus and finally terminate between and on the surface of the secretor cells. The vaso-motor fibers terminate between and on the muscle cells in the walls of the blood-vessels.

The local ganglion cells, however, are in anatomic relation with fine medullated nerve-fibers coming directly from the medulla oblongata and the spinal cord. As they enter the ganglia, their terminal branches arborize around and closely invest the cells of the ganglia and come into intimate histologic and physiologic connection with them. The nerve-fibers coming from the central nerve system are known as pre-ganglionic fibers, while those coming from the ganglia are known as post-ganglionic fibers. Through the intermediation, therefore, of the ganglion cells, the secretor cells of the salivary glands and the blood-vessels surrounding them are brought into relation with the central organs of the nerve system and become susceptible of being influenced by them.

The Parotid Saliva.—The parotid saliva, as it flows from the orifice of Stenson's duct, is clear, limpid, free from viscidity, distinctly alkaline in reaction, with a specific gravity of 1.003. Chemic analysis shows that it consists of water, a small quantity of protein matter, a trace of a sulphocyanogen compound, and inorganic salts. The secretion is increased during mastication, and especially on the side engaged in mastication. Dry food causes a larger flow than moist food. The situation of the orifice of the parotid duct is such that as the secretion is poured into the mouth it is at once incorporated with the food by the movements of the lower jaw, and thus fulfils the physical function of softening and moistening it.

The Submaxillary Saliva.—The submaxillary saliva is clear, slightly viscid, alkaline in reaction, and has a specific gravity of 1.002. It consists of water, protein matter (mucin), and inorganic salts.

The Sublingual Saliva.—The sublingual saliva is clear, extremely viscid, and strongly alkaline in reaction. It consists of water, protein matter (chiefly mucin), and inorganic salts.

The small racemose glands embedded in the mucous membrane on the inner surface of the cheeks and lips, on the hard and soft palate, and on the tongue and pharynx, secrete a fluid which is grayish in color, and extremely viscid and ropy. It contains a large amount of mucin.

Mixed Saliva.—The saliva of the mouth is a complex fluid composed of the secretions of all the salivary glands. As obtained from the mouth it is frothy, opalescent, slightly turbid, and somewhat viscid. The specific gravity is low, ranging from 1.000 to 1.006. The reaction is usually distinctly alkaline. It may, however, be neutral or even acid in reaction if there is any fermentation of food particles in the mouth or in certain disorders of the alimentary canal. When examined with the microscope, the saliva is seen to contain epithelial cells, salivary corpuscles resembling leukocytes, particles of food, and various microörganisms, especially *Leptothrix buccalis.*

The chemic composition of the saliva is shown in the following table:

COMPOSITION OF HUMAN SALIVA.

Water	995.16	994.20
Epithelium	1.62	2.20
Soluble organic matter	1.34	1.40
Potassium sulphocyanid	0.06	0.04
Inorganic salts	1.82	2.20
	1000.00	1000.04
	(Jacubowitsch.)	(Hammerbacher.)

Water constitutes the main ingredient, amounting to 99.5 per cent. The soluble organic matter is protein in character and is a mixture of mucin, globulin, and serum-albumin. The potassium sulphocyanid is mainly derived from the parotid gland. Its presence can be demonstrated by the addition of a few minims of a dilute solution of slightly acidulated ferric chlorid, when a characteristic red color is developed. The inorganic constituents comprise the sodium, calcium, and magnesium, phosphates, sodium carbonate, and sodium and potassium chlorids.

The relative amounts of the different constituents of the saliva will depend on the relative degree of activity of the different glands, and this in turn will be determined by the character of the food. When the food is dry, there will be an excess of the parotid secretion; when it partakes of the consistence of meat, there will be a larger secretion of the submaxillary saliva. The glands apparently adapt their activity to the character of the food.

Quantity of Saliva.—The estimation of the total quantity of mixed saliva secreted in twenty-four hours is exceedingly difficult, and the results obtained must be only approximative. It is, of course, subject to considerable variation, depending upon habit, the nature of the food, etc. The experiments of Professor Dalton and the results obtained by him are eminently trustworthy, and in all probability represent as nearly as possible the exact amount secreted. He found that without any artificial stimulus he was enabled to collect from the mouth about 36 grams (540 grains) of saliva per hour, but that upon the introduction of any stimulating substance into the mouth the quantity could be greatly increased. During mastication the saliva was poured out in greater abundance, the amount depending upon the relative dryness of the food. He found that wheat bread absorbed 55 per cent. of its weight, and fresh cooked meat 48 per cent. If, therefore, the average quantity of bread and meat required daily by a man of ordinary physical development and activity be assumed to be 540 grams (19 oz.) of the former and 450 grams (16 oz.) of the latter, these two substances would absorb respectively 297 grams (4573.8 grains) and 216 grams (3326.4 grains), making a total of 513 grams (7900 grains). If, therefore, the amount secreted and mixed with the food during an estimated two hours of mastication be added to the amount secreted during the remaining twenty-two hours, supposing that it continues at the rate of 36 grams per hour, we have a total amount of 513 + 792 grams, or 1305 grams (19,780 grains), or about 2.8 pounds.

Histologic Changes in the Salivary Glands during Secretion.—During and after secretion very remarkable changes take place in the cells lining the acini, which are in some way connected with the production of the essential constituents of the salivary fluids. In the case of the parotid gland, which may be regarded as the type of a serous or albuminous gland, the following changes have been observed by Langley (Fig. 66). During the period of rest and just previous to secretor activity, the epithelial cells are enlarged and swollen, and encroach on the lumen of the acinus. The protoplasm of the cells is so completely filled with dark fine granules as not only to obscure the nucleus, but almost to obliterate the line of union of the cells. As soon as secretion becomes active, however, the granules begin to disappear from the outer region of the cell and move toward the inner border and into the lumen of the acinus. From these observations it might be inferred that during rest the protoplasm of the cells gives rise to granular material, and that during and after secretor activity there is an absorption of new material from the lymph and a reconstruction of the granular material.

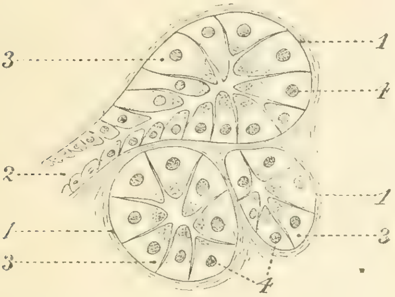

Fig. 66.—Parotid Gland After Prolonged Activity. 1,1, Acini; 2, duct; 3,3, albuminous cells almost free of granules; 4, nuclei clear and well defined. (Semi-diagrammatic.)

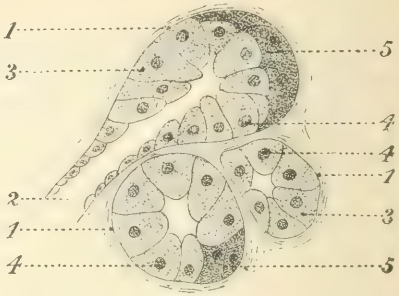

Fig. 67.—Submaxillary Gland After Prolonged Activity. 1,1, Acini; 2, duct; 3,3, mucous cells free of mucin and filled with fine granules; 4,4, nuclei rounded and returned to the center of the cell; 5,5, cells of Giannuzzi, large and distinct. (*After Vialleton.*)

In the submaxillary gland, a portion of which may be taken as a type of a mucous gland, similar changes have been observed (Fig. 67). During rest the epithelial cells are large, clear in appearance, highly refractive, and loaded with small globules resembling mucin. The nucleus, surrounded by a small quantity of protoplasm, lies near the margin of the cell. That the granules are not protoplasmic in character is shown by the fact that they do not stain on the addition of carmine. When treated with water or dilute acids, the globules swell, coalesce, and form a uniform mass. The chemic relations of this substance indicate that it is the precursor of mucin—namely, mucigen. During secretor activity the cells discharge these mucigen granules into the lumen of the acinus where they are transformed into mucin. Though the appearance of the gland-cell indicates it, there is no evidence for the view that the cell itself undergoes disintegration in the process.

The Physiologic Actions of Saliva.—The constant presence of salivary glands in the different classes of animals and the large amount of secretion they pour daily into the alimentary canal point to the conclusion that this mixed fluid plays an important rôle in the general digestive process. Experiment has demonstrated that it has a two-fold action; viz., physical and chemical.

Physically, saliva softens and moistens the food, unites its particles into a consistent mass by means of its contained mucin, and thus facilitates swallowing.

Chemically it converts starch into sugar. This action is more marked with boiled than with raw starch, a fact which depends on the physical structure of the starch grain. In the natural condition each starch grain consists of a cellulose envelope or stroma in the meshes of which is contained the true starch material, the granulose. When boiled for some minutes, the starch grain absorbs water, the granulose swells and ruptures the cellulose envelope, after which it passes into an imperfect opalescent solution more or less viscid, depending on the relative amounts of water and starch. This is the change largely brought about by the process of cooking. If a portion of this hydrated starch be kept in the mouth for a few minutes it will be converted into sugar, a fact made evident by the sense of taste.

The chemic action of saliva in converting starch into sugar, as well as the intermediate stages, can be experimentally shown in the following manner: To 5 volumes of a thin starch solution in a test-tube add two volumes of filtered saliva. Place the mixture in a water-bath at a temperature of 35° C. In a few minutes the starch passes into a soluble condition and the fluid becomes clear and transparent. On testing the solution from time to time with iodin the characteristic blue reaction will be found to disappear, gradually, the color passing from blue to violet, to red, to yellow. If now the solution be boiled with a solution of cupric hydroxid (Fehling's solution) a copious red or yellow precipitate of cuprous oxid is formed, which indicates the presence of sugar. The polariscope shows that this sugar is dextrorotatory. During the conversion of the starch intermediate substances are formed to which the term dextrin is applied. After the starch has been rendered soluble it undergoes a cleavage into maltose and a dextrin, which, as it gives rise to a red color with iodin, is termed erythrodextrin. At a later stage this erythrodextrin also undergoes a cleavage into maltose and a second variety of dextrin, which, as it does not give rise to any color with iodin, is termed achroödextrin. It is claimed by some investigators that this form can also in time be transformed into sugar. It is possible that a small quantity of dextrose is also formed.

The successive stages of the conversion of starch into sugar may be represented by the following schema:

$$\text{Starch} = \text{Soluble Starch} = \begin{cases} \text{Erythrodextrin} = \begin{cases} \text{Achroödextrin.} \\ \text{Maltose.} \end{cases} \\ \text{Maltose.} \end{cases}$$

This change consists in the assumption by the starch of a molecule of water, and for this reason the process is termed hydrolysis. The nature of the chemic change is shown in the following formula:

$$\begin{gathered} 3(C_6H_{10}O_5) + H_2O = C_{12}H_{22}O_{11} + C_6H_{10}O_5 \\ \text{Starch} + \text{Water} = \text{Maltose} + \text{Dextrin.} \end{gathered}$$

The amylolytic[1], amyloclastic, or starch-changing action of saliva depends on the presence of an unorganized ferment or enzyme known as *ptyalin* or *amylase*. This enzyme is present in the secretion of each of the salivary glands. The chemic character of ptyalin is unknown, though there are reasons for believing that it partakes of the nature of a protein. It is a product in all probability of the katabolic activity of the secretor cells. According to Latimer and Warren, ptyalin is a derivative of the zymogen, ptyalogen. This latter compound has been shown to be present in the glands of the dog, cat, and sheep. Ptyalin effects the transformation of starch merely by its presence, and undergoes no perceptible consumption in the process. The activity of this enzyme is very great, and unless interfered with by an excess of sugar and dextrin, it acts practically indefinitely.

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[1] The term amylolytic has been objected to on the ground that it does not correctly express the fact, but is analogous with electrolytic and means a transformation by means of starch. Armstrong has suggested the use of the term amyloclastic as well as proteoclastic and lipoclastic for the terms now generally employed.

The activity of ptyalin is modified by various external conditions, among which may be mentioned the chemic reaction of the medium in which it is placed. It is most active when the medium is moderately alkaline. Its activity is arrested by strong alkalies or acids, though the presence of a small percentage of an acid does not appear to have any effect in either hastening or retarding the process. This fact has a bearing upon the question as to whether the action of the saliva is interfered with in the stomach by the presence of the gastric juice. At present it is a disputed matter, but the weight of authority is in favor of the view that the transforming action may continue for almost half an hour during the early stages of gastric digestion. The temperature also influences the rapidity with which the transformation of the starch is effected. At a temperature of 95° to 106°F. the ptyalin acts most energetically, while its activity is entirely arrested by reducing the temperature to the freezing-point or raising it to the boiling point.

The Mode of Secretion of Saliva.—The secretion of saliva is a complex act and involves the coöperation of gland-cells, blood-vessels, efferent and afferent nerves contained in different cranial nerves, and a central mechanism by which they are excited to and coördinated in activity. The central mechanism is located in the medulla oblongata in the gray matter beneath the floor of the fourth ventricle and subject to cerebral and surface stimulation.

During the intervals of mouth digestion the glands are practically at rest as far as the *discharge* of saliva is concerned. The cells, however, are actively engaged in absorbing from the surrounding lymph-spaces materials derived from the blood, out of which they construct their characteristic constituents. The blood-vessels possess that degree of dilatation necessary for nutritive purposes.

With the development of the sensation of hunger, the sight and the odor of agreeable foods develop visual and olfactory sensations, which give rise to psychic states more or less agreeable. With their development the entire mechanism is excited to activity and a more or less abundant discharge of saliva into the mouth frequently takes place. This is, therefore, known as a *psychic* secretion. The fluid thus secreted has given rise to the expression "watering of the mouth."

With the introduction of food into the mouth and the stimulation of afferent nerves (nerves of general sensibility and nerves of taste) and the onset of mastication, the blood-vessels suddenly dilate, the blood-supply is increased, and the gland-cells begin to discharge water, inorganic salts, and their organic constituents into the lumen of the acinus, materials that collectively constitute the saliva characteristic of any one of the glands. This continues until mastication ceases, when all the structures return to their former condition of relative inactivity.

The Nerve Mechanism of Insalivation.—The nerves and nerve-centers that constitute the nerve mechanism for the secretion of saliva, as determined by experimental investigations are shown in the following table:

Afferent Nerves.	Nerve-centers.	Efferent Nerves.
1. Lingual and buccal branches of the trigeminal nerve.	Medulla oblongata.	The chorda tympani and its post-ganglionic continuations for the submaxillary and sublingual glands; the glosso-pharyngeal nerve and its post-ganglionic continuations contained in the auriculo-temporal branch of the trigeminal nerve, for the parotid gland.
2. Taste fibers in the chorda tympani.		
3. Taste fibers in the glosso-pharyngeal.		The sympathetic nerve, both pre- and post-ganglionic fibers, for all the glands.

The Efferent Nerves.—The efferent nerve-fibers, as stated in the foregoing paragraph, that transmit nerve impulses to the submaxillary, sublingual, and parotid glands, as well as to their associated blood-vessels, belong to the autonomic system, and are contained respectively in the chorda tympani and its post-ganglionic continuations, in the glosso-pharyngeal and its post-ganglionic continuations contained in the auriculo-temporal branch of the fifth nerve, and in the *post-ganglionic* branches of the sympathetic nerve derived from the superior cervical ganglion. That these nerves transmit the nerve impulses to the salivary apparatus is shown by the effects that follow their division and stimulation.

The Chorda Tympani.—The chorda tympani nerve is apparently a branch of the facial (though it consists in part of autonomic nerve-fibers), the trunk of which it leaves in the aqueduct of Fallopius. It then crosses the tympanic cavity, emerges through the Glaserian fissure, and joins the lingual branch of the inferior maxillary division of the fifth nerve. After passing forward as far as the sublingual gland, nearly all of the fibers leave the lingual nerve by four or five strands to become connected by terminal branches with nerve ganglion cells in relation with the submaxillary and sublingual glands. (See Fig. 68.)

The effects on the secretion and flow of saliva from the submaxillary gland which follow division and stimulation of the chorda tympani nerve are shown in the following way: A cannula is inserted into Wharton's duct and the rate of flow estimated; the nerve is then divided, after which the flow ceases. The peripheral end of the nerve is then stimulated with induced electric currents when a copious secretion of a thin saliva takes place, accompanied by a marked dilatation of the blood-vessels of the gland. The quantity of blood passing through the vessels is so great as to give to the venous blood an arterial hue and to the small veins a distinct pulsation. It would appear from these effects that the chorda contains two sets of fibers, one of which inhibits the action of a local vaso-motor mechanism permitting the blood-vessels to dilate (vaso-dilatator fibers), the other of which stimulates the secretor cells to activity, through the intermediation of local ganglia.

That local ganglia are involved is shown by the effects which follow the injection of nicotin into the circulation. After a sufficient dose—10 milligrams for the cat—stimulation of the chorda has no effect. Stimulation of the nerve-plexus beyond the ganglion, the post-ganglionic fibers, however, is at once followed by vascular dilatation and secretion, a fact that would indicate that the ganglia are not only stimulated by the chorda tympani but that the conductivity of the nerve endings of the chorda around the ganglia is impaired.

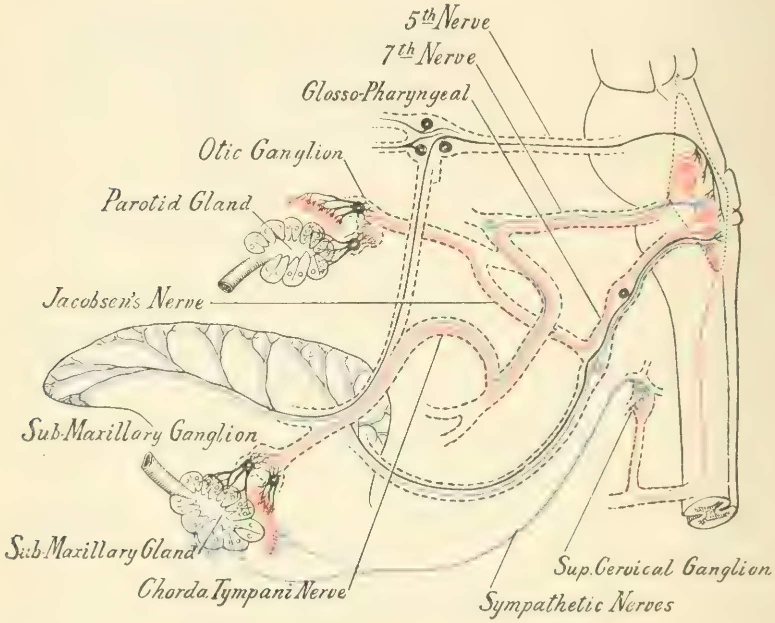

Fig. 68.—Scheme of the Nerves Involved in the Secretion of Saliva.

It might be inferred that the increase in the flow of saliva is due to filtration, the result of the increased blood-supply to the gland, and not to the influence of any true secretor fibers stimulating the activities of the secretor cells. That this is not the case, however, can be demonstrated in several ways: first, the pressure in the duct of the submaxillary gland, as shown by the mercurial manometer, rises, when the gland is secreting, considerably above the pressure in the carotid artery, which could not be the case if it were due to a mere filtration; for if pressure alone were the cause, the flow of saliva would cease as soon as the pressure in the tube equaled the pressure in the blood-vessels. Second, even in the absence of blood the gland can be made to yield a secretion, as shown by stimulating the nerve in a recently killed animal. Third, after the injection of atropin into the circulation the secretion is abolished, but the local vaso-motor mechanism is unimpaired, for stimulation of the nerve, as in the previous instance, gives rise to a dilatation of the vessels and an increased blood-supply. There is thus abundant proof that the chorda tympani contains two sets of fibers—one regulating the blood-supply to the gland, the other stimulating the secretor cells.

The efferent fibers, vaso-motor and secretor, which constitute in part the chorda tympani nerve have their origin in cells, the *nucleus salivatorius*, located beneath the floor of the fourth ventricle, from which they emerge in the nerve of Wrisberg or pars intermedia, and enter the trunk of the facial nerve at the bottom of the internal auditory canal after which they pursue the course stated above.

The Glosso-pharyngeal Nerve.—The autonomic nerve-fibers that conduct nerve impulses outward from the medulla to the parotid gland are believed to pass through the glosso-pharyngeal nerve, through the tympanic branch or nerve of Jacobson, to the otic ganglion, with which they become connected. From this ganglion new nerve-fibers arise which pass into the fifth nerve and reach the secretor cells of the parotid gland through the auriculo-temporal nerve. The trunk of this latter nerve contains therefore post-ganglionic fibers that bear the same relation to the parotid gland and blood-vessels that the post-ganglionic fibers from the submaxillary ganglion bear to the submaxillary gland and blood-vessels.

The influence of the efferent fibers in the trunk of the glosso-pharyngeal on the parotid gland is similar to the influence of the chorda tympani on the submaxillary gland; for if the glosso-pharyngeal nerve or its post-ganglionic continuations in the auriculo-temporal nerve be stimulated in any part of its course with induced electric currents there follows a dilatation of the blood-vessels and an abundant discharge of a thin saliva rich in water and salts but poor in the amount of organic matter. Division of the glosso-pharyngeal nerve, extirpation of the otic ganglion or division of the auriculo-temporal nerve is followed by a loss of reflex secretion. Stimulation of the branch connecting the glosso-pharyngeal with the otic ganglion (Jacobson's nerve) gives rise to the secretion as shown by Heidenhain. Division of the nerve is also followed by a loss of reflex secretion.

The Sympathetic Nerves.—The autonomic nerve-fibers which influence the salivary secretion emerge from the spinal cord mainly through the second, third, and fourth thoracic nerves. After passing into the sympathetic chain they ascend to the superior cervical ganglion, with the cells of which they become connected through the intermediation of fine terminal branches. From this ganglion non-medullated nerve-fibers—sympathetic nerves proper—follow the branches of the external carotid artery to the different glands. There is no evidence that these fibers have any connection, anatomic or physiologic, with local ganglia at or near the submaxillary, sublingual, or parotid glands. If the sympathetic nerve in the neck, especially in the dog, be divided and the peripheral end stimulated with induced electric currents, there is at once a contraction of the smaller blood-vessels of the submaxillary and sublingual glands and a diminution of the blood-supply, a result showing the presence of vaso-constrictor fibers. Nevertheless both the submaxillary and sublingual glands pour out a saliva which is different from that poured out when the chorda tympani is stimulated. The quantity is less, it is more viscid, richer in organic matter, of a higher specific gravity, and more active in the transformation of starch into sugar.

Stimulation of the sympathetic fibers passing to the parotid gland is followed by contraction of the vessels and an abolition of the secretion; but at the same time there is an increased activity of the secretor cells, for subsequent stimulation of the auriculo-temporal nerve not only causes an increase in the amount of water and inorganic salts, but an increase also in the amount of organic matter far beyond that produced when the auriculo-temporal alone has been stimulated. Histologic examination shows that the small ducts of the gland are filled with thick organic matter after stimulation of the cervical portion of the sympathetic chain.

The foregoing facts led Heidenhain to the conclusion that there are two physiologically distinct efferent nerve-fibers distributed to the glands, viz., *trophic* nerves, derived from the sympathetic which stimulate the cells to the production of organic constituents; and *secretor* nerves, derived from the cranial nerves, chorda tympani and glosso-pharyngeal, which stimulate the cells to the production of water and inorganic salts. This view has, however, been controverted by Langley, who regards the secretor fibers to the glands as essentially the same, and considers the differences in the character of the secretion to be dependent on differences in the quantity of the blood-supply induced by the simultaneous stimulation of the vaso-motor nerves.

The Central Mechanism.—The central mechanism that excites the glands and blood-vessels to activity through efferent nerves originating in its cells may be aroused to action (1) by nerve impulses descending from the cerebrum in consequence of psychic states induced by the sight or the odor of foods especially after long abstinence; (2) by nerve impulses transmitted through afferent nerves from the mouth, developed by the contact of the food with the peripheral terminations of the gustatory or general sensor nerves.

That psychic states, ideas and feelings aroused by the sight, odor, and contemplation of food can give rise to a stimulation of the cells of the central mechanism in the manner just stated is shown by the flow of saliva which is familiarly known as watering of the mouth. This fact has been experimentally demonstrated by Pavlov on dogs. This investigator caused the ducts of the glands to be brought to the surface in such a manner that they healed into the edges of the skin wounds. By means of suitable receivers applied over the orifices of the ducts the saliva could be readily collected. When the dog under such circumstances was tempted by the sight of foods there was at once a free discharge of saliva, the quantity and quality of which varied with the character of the foods.

That the central mechanism can be excited to activity by nerve impulses reflected from the periphery can be demonstrated by the introduction of food into the mouth, as well as by stimulation of the branches of the afferent nerves distributed to the mouth which constitute the afferent part of this mechanism.

The Afferent Nerves.—The afferent nerves that transmit nerve impulses from the mouth to the central mechanism, are the taste fibers in the chorda tympani, the taste and sensor fibers of the glosso-pharyngeal, and the sensor fibers of the lingual and buccal branches of the trigeminal nerve. This is shown by the fact that if they are transversely divided there is a cessation of the discharge of saliva when the peripheral nerve endings in the mouth are stimulated by the presence of food. With these nerves intact the introduction of food into the mouth will invariably be followed by a flow of saliva. Pavlov has apparently demonstrated that this general fact must be supplemented by the further fact, that there is a special adaptation between the character of food and the different glands. Thus, solid dry foods, cause a large flow of a thin saliva from the parotid glands, but a slight flow from the submaxillary; moist foods and especially meat causes a large flow from the submaxillary gland, but a slight flow from the parotid. It is also probable that the glands respond by discharging a secretion of special quality in accordance with the properties of the different foods.

Stimulation of the afferent nerves with induced electric currents also gives rise to a discharge of saliva. This can be demonstrated by exposing the glands and the afferent nerves and subjecting them to experiment. Under such circumstances, if a cannula be placed in the duct of the submaxillary gland, and the lingual nerve stimulated by induced electric currents of moderate strength, a copious flow of saliva at once takes place. If now the glosso-pharyngeal nerve or the central end of the divided chorda tympani nerve be stimulated in a similar manner, the effect on the secretion will be the same. Division of these nerves in an animal, in such a way as to prevent the nerve impulses from reaching the medulla oblongata, is followed by a marked diminution in the amount of saliva secreted. The reflex centers, however, may receive impulses and be excited to activity by impulses coming through other nerves—*e.g.*, the pneumogastric, when the mucous membrane of the stomach is stimulated; the sciatic, when after division, its central end is stimulated.

Résumé of the Factors Involved in the Secretion of Saliva.—From the foregoing statements it is apparent that the secretion of saliva is a complex act involving the coöperation of several different factors. As the mechanism for the elaboration of this secretion is typical of that for many secretions it will be of advantage to summarize these factors and their specific functions. These are as follows:

1. *Epithelial cells*, the physiologic actions of which are the production of the specific characteristic constituents of the saliva, *e.g.*, mucin, albumin, the enzyme ptyalin, as well as the absorption and discharge of water and inorganic salts.
2. *Lymph*, which contains the nutritive material necessary for the growth, repair, and metabolic activities of the secreting cells.
3. *Capillary blood-vessels*, which permit the passage of those constituents of the blood that collectively constitute lymph.
4. *Vaso-motor nerves*, some of which at the beginning of secretor activity dilate the blood-vessels and thus increase the blood-supply and the production of lymph (vaso-dilatator nerves); others of which at the end of secretor activity perhaps actively contract the blood-vessels and thus decrease the blood-supply to the previous condition (vaso-constrictor nerves).
5. *Secretor nerves*, which stimulate the epithelial cells to increased activity causing them to discharge their specific metabolic constituents along with water and inorganic salt in characteristic proportions from the orifices of the gland ducts (secreto-motor nerves).

The central mechanism is excited to coördinate activity, primarily, by nerve impulses descending from the cerebrum as a result of psychic states developed by the sight and odor of food, and secondarily, by nerve impulses, transmitted by the nerves of gustation and general sensibility and developed by the contact of food on their peripheral terminations during the act of mastication.

Modifications of the Nerve Mechanism of Insalivation due to the Physiologic Action of Drugs.—The functions of different portions of the nerve mechanism of insalivation may be made apparent by an analysis of the effects that follow the administration of physiologic or slightly toxic doses of the alkaloids of various drugs. The effects can be shown to be due to a depression or stimulation of the normal activity of one or more portions of the mechanism. As a result the secretion may be decreased or increased in volume. The following examples will illustrate the action of alkaloids in general.

Nicotin.—When nicotin in sufficiently large doses is given to an animal hypodermatically, the secretion of saliva after a variable period of time ceases and the mouth becomes dry. If the chorda tympani nerve, *i.e.*, the preganglionic portion, be then stimulated with induced electric currents the usual phenomenon, viz., a free flow of saliva, fails to occur. If, however, the nerve branches emerging from the submaxillary ganglion, *i.e.*, the postganglionic portion, be stimulated with electric currents, the saliva will be discharged as usual. The inference is that the conductivity of the peripheral terminations of the preganglionic chorda fibers is depressed so that the nerve impulses discharged by the central mechanism fail to reach, and therefore to stimulate, the submaxillary ganglion cells. The inference as to the seat of action of nicotin is supported by the fact that painting the surface of the superior cervical sympathetic ganglion with nicotin will impair the conductivity of the terminal branches of the pre-ganglionic fibers emerging from the cord so that stimulation of these fibers fails to produce beyond the ganglion the usual secretor effects. It is probable that nicotin has a similar action on the peripheral terminations of Jacobson's nerve which arborize around the nerve cells of the otic ganglion.

Atropin.—Atropin in doses of 1 milligram also causes a complete cessation in the flow of saliva and consequently an extreme dryness of the mouth. After the occurrence of this condition neither stimulation of the pre-ganglionic chorda tympani fibers nor of the post-ganglionic fibers, will cause the glands to secrete. But as stimulation of the sympathetic nerve in the cervical region will excite a secretion the inference is that the atropin exerts a depressing effect on the conductivity of the nerve endings in contact with the gland cells thus interfering with the transmission of nerve impulses, rather than on the gland cells themselves. The same holds true for the nerve terminations in the post-ganglionic fibers distributed to the parotid gland. The action of atropin is not limited, however, to the nerve terminations in connection with salivary glands but extends to the nerve terminations in connection with many other glands in the alimentary canal and skin. Even though the dose of atropin be large, 10 to 15 milligrams for a dog, its action is confined to the terminal nerve-fibers in connection with the gland cells, for when the chorda tympani is stimulated the blood-vessels around the gland dilate as usual, a fact which indicates that the submaxillary ganglion gives off fibers of a vaso-dilatator as well as a secretor character. Unless the dose of atropin be largely increased, *e.g.*, 100 milligrams, it fails to depress the conductivity of the terminals of the sympathetic nerve-fibers.

Pilocarpin.—Pilocarpin in small doses, from 2 to 5 milligrams, hypodermatically causes in the cat a free flow of saliva which may amount to half a liter or more in the course of several hours. In human beings its effect on the flow of saliva is equally marked. Ringer reports that in two patients, after taking a medicinal dose, the amount of saliva discharged was 622 c.c.

and 764 c.c. respectively. Since division of the nerves both pre- and post-ganglionic, does not diminish or abolish the secretion, the inference is that the pilocarpin exerts a stimulating action on the nerve endings in connection with the gland cells. This inference is strengthened by the fact that the pilocarpin effect is antagonized and the secretion checked by a suitable dose of atropin, the seat of the action of which is known. The two alkaloids thus appear to be in physiologic antagonism in their action on these nerve terminations. The action of pilocarpin is not limited to the salivary glands, but extends to glands found in the alimentary canal, respiratory passages, and skin.

DEGLUTITION

Deglutition is that part of the digestive process which is concerned in the transference of the food from the mouth through the pharynx and esophagus into the stomach. This is an extremely complex act and involves the action of a large number of structures, all of which are made to act in proper sequence under the coördinating influence of the nerve system. The deglutitory canal consists of the mouth, pharynx, and esophagus, each of which presents certain anatomic features on which its physiologic action depends.

The Mouth.—The cavity of the mouth is bounded in front and on the sides by the alveolar arches and the teeth; the roof is formed by the hard palate and the floor by the tongue. Anteriorily, the mouth communicates with the exterior by a transverse opening the buccal orifice, and posteriorly with the pharynx by an opening, the isthmus of the fauces. The cavity of the mouth is lined by mucous membrane in which are imbedded numerous mucous glands. The interior of the mouth is separated in part from the interior of the pharynx by an incomplete septum formed above by the soft palate, laterally by the anterior and posterior palatal arches and below by the tongue.

The Pharynx.—The pharynx is an oval-shaped cavity extending from the base of the skull to the lower border of the cricoid cartilage, a distance of about 12 centimeters. Its walls are formed mainly by three pairs of muscles—the superior, middle, and inferior constrictors—each consisting of red, striated muscle-fibers, and hence capable of rapid and energetic contractions. Superiorly the pharynx is attached to and supported by the basilar process of the occipital bone; inferiorly it becomes continuous with the esophagus. The anterior wall of the pharynx is imperfect and presents openings which communicate with the nasal chambers, the mouth, and the larynx. The lateral wall on either side presents the opening of the Eustachian tube which leads directly into the cavity of the middle ear. The interior of the pharynx is lined by mucous membrane. The pharynx is partially separated from the mouth by the velum pendulum palati, a muscular structure attached above to the hard palate; its lower edge or border is directed downward and backward and presents in the middle line a conical process, the uvula. On either side the palate presents two curved arches, the anterior and posterior, formed respectively by the palato-glossei and palato-pharyngei muscles. The superior laryngeal aperture is placed just beneath the base of the tongue. It is triangular in shape, wide in front, narrow behind, and directed downward and backward. It is bounded above by a thin plate of cartilage, *the epiglottis*, placed just behind the tongue and so arranged that it can easily be depressed and elevated.

The Esophagus.—The esophagus, the continuation of the deglutitory canal, extends downward from the lower border of the cricoid cartilage for a distance of from 22 to 25 centimeters, to a point opposite the ninth thoracic vertebra, where it expands into the stomach. Its walls are composed of an internal or mucous and an external or muscle coat, united by areolar tissue. The muscle coat consists of an external layer of longitudinal fibers arranged in three bands and of an internal layer composed of fibers arranged circularly in the upper part and obliquely in the lower part of the esophagus. In the upper third the fibers are striated; in the middle third they are a mixture of both striated and non-striated; in the lower third they are entirely non-striated.

The muscle-fibers surrounding the esophago-gastric orifice are arranged in the form of and play the part of a sphincter muscle, and for this reason may be termed the *sphincter cardiæ* muscle. By its action it prevents a return under normal conditions of food into the esophagus.

The deglutitory act may be for convenience divided into three stages, viz.:

1. The passage of the food from the mouth into the pharynx.
2. The passage of the food through the pharynx into the esophagus.
3. The passage of the food through the esophagus into the stomach.

In the first stage the bolus of food is placed on the superior surface of the tongue. The mouth is then closed and respiration is momentarily suspended. The tip of the tongue is placed against the posterior surfaces of the teeth. The tongue, by reason of its intrinsic musculature, then arches from before backward against the roof of the mouth and by the contraction of the hyoglossus muscle pushes the bolus of food through the isthmus of the fauces into the pharynx. This completes the first stage. It is a voluntary effort and accomplished partly by the tongue, though, as shown by Meltzer, mainly by the mylohyoid muscles.

The second and third stages, or the passage of the food through the pharynx and esophagus into the stomach, have been attributed until quite recently entirely to peristaltic movements of their musculature.[1] It has been stated that with the passage of the food through the isthmus of the fauces the posterior wall of the pharynx advances and seizes the food, which, in consequence of a rapid peristaltic movement running through the constrictor muscles from above downward is transferred to the esophagus; that with the entrance of the food into the esophagus a similar peristalsis, varying in rapidity in different sections in consequence of a change in the character of its musculature, gradually transfers the food into the stomach. There can be but slight doubt that by this method the bolus of food, especially if it is of firm consistence and of a size sufficient to distend the esophagus, is transferred into the stomach, but that it is not the case with liquids has been demonstrated by Kronecker, Falk, and Meltzer.

In 1880 the first of these experimenters made the observation that the sensation in the stomach following the swallowing of a mouthful of cold water occurred too quickly to be explained by the prevalent belief that its transference was caused by ordinary peristalsis, the rate of progression of which was known to be slow. Falk then discovered the fact, by introducing through the mouth into the pharynx a tube connectedexternally with a water manometer, that during the act of swallowing there is a sudden rise of pressure equal to about twenty centimeters of water.

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[1] Peristalsis may be defined as a progressive wave-like movement which passes over different portions of the walls of the alimentary canal. Its effect physiologically is the propulsion of its solid and semisolid contents. It is characterized by a contraction of the muscle-fibers behind the object and an inhibition or relaxation of the muscle-fibers in front of it. (Bayliss and Starling.)

These experiments demonstrated that at the beginning of deglutition there is a sudden rise of pressure, the result of a quickly acting force resident in the mouth or pharynx, in consequence of which the liquid foods are rapidly thrown down toward the end of the esophagus, peristalsis playing no part in the process. The proof, however, of these statements was furnished by Meltzer. This observer introduced into the pharynx and esophagus rubber tubes, the ends of which were provided with thin-walled rubber balloons which could be distended with air. The outer ends of the tubes were connected with Marey's recording tambours. Any compression of the balloon would be followed by the passage of the air into the tambour and an elevation of the lever. With one balloon in the pharynx and the other in the esophagus at varying depths, and the recording levers of the tambours applied against the surface of a revolving cylinder, it became possible, with the addition of a chronograph, to obtain a graphic representation of the time relations of simultaneous and successive compressions of the two balloons.

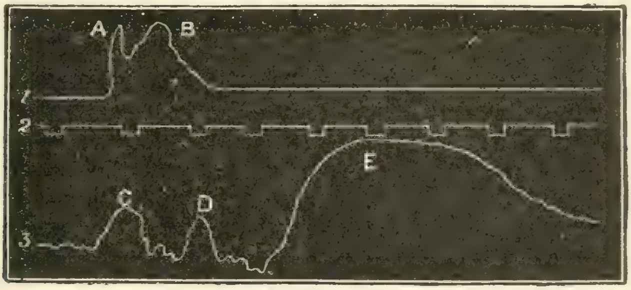

FIG. 69.—TRACING OF THE ACT OF DEGLUTITION. 1. A indicates the compression of the elastic bag caused by the bolus projected by the contraction of the mylohyoid muscles. B. Contraction of the pharynx. 2. Line marking seconds. 3. Tracing of the bag in the esophagus 12 cm. from the teeth. C. Compression of the bag by the bolus corresponding to A. D. Compression by the residues of the bolus carried on by the contraction of the pharynx, B. E. Contraction of the esophagus.—(*Landois and Stirling.*)

It was found as the result of many experiments that no matter how deep the position of the esophageal balloon, it was compressed almost simultaneously with the pharyngeal balloon, as shown by the rise of the levers on swallowing a mouthful of water. The interval of time between the rise of the two levers did not amount to more than the tenth of a second. The inference was that the water was projected or shot down the pharynx and esophagus in this period of time, and in its passage compressed both balloons practically at the same instant. The same was found to be true when small masses of more consistent food were swallowed.

The curves of the entire deglutitive act recorded by the two levers are, however, different in form. (See Fig. 69.) The pharyngeal curve, 1, presents two crests, the first, A, being due to the compression caused by the passage of the bolus, the second, B, due to the compression exerted by the contraction of the pharyngeal muscles. The interval of time between these two crests amounts to not more than 0.3 second. In the esophageal curve, 3, the elevation, C, corresponds to the elevation, A, and is likewise due to the compression exerted by the bolus. The interval of time between the beginning of the first and second curves was not more than 0.1 second, regardless of the depth to which the esophageal balloon was plunged. At a later period a second rise of the lever was recorded; the time of its appearance, height, duration, etc., were found to increase with the depth of the balloon.

These facts demonstrate that deglutition consists of two phases: (1) a rapid rise of pressure in the pharynx, as a result of which liquid or semiliquid foods are suddenly shot down to the lower end of the esophagus; (2) a peristaltic contraction of the musculature of the canal, which, acting as a supplementary force, carries onward any particles of food in the canal and forces the bolus through the closed *sphincter cardiæ* at the end of the esophagus.

The immediate cause of the sudden rise of pressure was shown by Meltzer to be the contraction of the mylohyoid muscles. When the nerves going to these muscles were divided in a dog, deglutition was practically abolished. These muscles are probably assisted in their action by the contraction of the hyoglossus muscles as well as the tongue itself.

The time required for a mouthful of liquid food to pass to the lower end of the esophagus is approximately about 0.1 second. If the cardiac orifice is normally closed, a period of about 6 or 7 seconds may elapse before the oncoming peristaltic wave reaches the end of the esophagus and forces the fluid into the stomach. If, however, a series of deglutitory acts follow one another in quick succession there is an inhibition of the cardiac sphincter and the peristaltic wave until after the last swallow. The time required for the food to pass down the esophagus and into the stomach may vary in different animals and in different human beings.

An examination of the action of the esophagus during deglutition, made by Cannon and Moser with x-rays and the fluoroscope, disclosed the fact that the method of food transmission varied in different animals. In the cat and dog the transmission was effected by peristalsis alone. The time required for the food to reach the stomach varied in the cat from nine to twelve seconds and in the dog from four to five seconds. The descent of the bolus was more rapid in the upper than in the lower part of the esophagus. In man, liquids descended rapidly, at the rate of several feet a second, in consequence of the rapid and energetic contraction of the mylohyoid muscles. A peristaltic contraction, passing over the entire esophagus, was necessary to the passage of solid and semisolid food through it.

Closure of the Posterior Nares and Larynx.—Because of the rapid rise of pressure in the deglutitory canal during the act of swallowing it is essential that the openings into the nasal and laryngeal cavities be closed to prevent the entrance of food into them, which would otherwise take place. Under normal circumstances this is done so effectually that it is seldom that any portion of the food, liquid or solid, ever enters the nasal chambers or the cavity of the larynx. The mechanism by which these openings are closed is as follows:

At the moment the food passes into the pharynx the posterior nasal openings are closed against the entrance of the food by a septum formed by the pendulous veil of the palate and the posterior half arches. The palate is drawn upward and backward by the *levator palati* muscles, until it meets the posterior wall of the pharynx, which at this moment advances. At the same time it is made tense, by the action of the *tensor palati* muscles. (Fig. 70). This septum is completed by the advance toward the middle line of the posterior half arches caused by the contraction of the muscles, the *palato-pharyngei*, which compose them. When these structures are impaired in their functional activity, as in diphtheritic paralysis and ulcerations, there is not infrequently a regurgitation of food, especially liquids, into the nose.

The larynx is equally protected against the entrance of food during deglutition under normal circumstances. That this accident occasionally happens, giving rise to severe spasmodic coughing, and even in extreme cases to suffocation, is abundantly shown by the records of clinical medicine. Usually it does not occur, for the following reasons: just preceding and during the act of deglutition there is a complete suspension of the act of inspiration, by which particles of food might otherwise be drawn into the larynx; at the same time the larynx is always drawn well up under the base of the tongue and its entrance closed by the downward and backward movement of the epiglottis, the result of the contraction of the aryteno-epiglottidean muscle.

The action here attributed to the epiglottis has been denied by Stuart and McCormick. These observers had the opportunity of looking into a naso-pharynx which had been laid open by a surgical operation for the removal of a morbid growth. In this patient, the epiglottis, at the time of deglutition, was always more or less erect and closely applied to the base of the tongue. So complete was this that the food passed over its posterior or inferior surface for a certain distance. In no instance was it ever observed to fold backward like a lid.

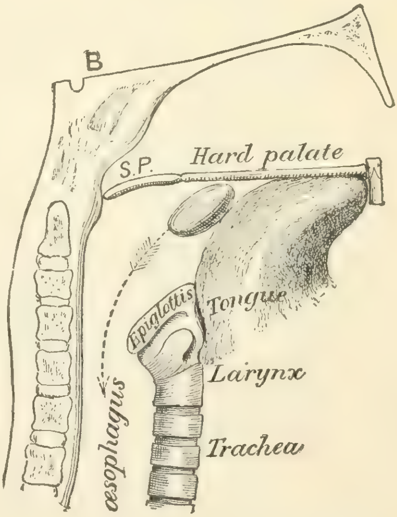

FIG. 70.—DIAGRAM SHOWING THE MANNER OF CLOSURE OF THE POSTERIOR NARES AND LARYNX DURING DEGLUTITION.— (*Landois and Stirling.*)

Because of the possibility that this position of the epiglottis was due to pathologic causes, Kanthack and Anderson instituted a new series of experiments with a view of determining the action of the epiglottis. As a result of many experiments on animals and of observations on themselves, these observers reaffirm the generally accepted view, that under normal conditions, the entrance of the larynx is always closed by the epiglottis after the manner of a lid.

In addition to the downward and backward movement of the epiglottis and the ascent of the larynx under the base of the tongue, it is also certain from the observations of Meltzer that the larynx is protected from the entrance of food, in the rabbit at least, by the closure of the glottis itself. This experimenter noticed, while observing the interior of the larynx, both from above, through an opening in the hyothyreoid membrane, and from below, through an opening in the trachea, that when an act of deglutition was excited by touching the soft palate with a sound, there was simultaneously with the contraction of the mylohyoid muscles, a firm closure of the glottis. This was accomplished by an approximation of the true vocal bands, a close approximation and a downward and forward movement of the arytenoid cartilages, until they almost touched the anterior wall of the thyroid cartilage. This movement preceded the ascent of the larynx. When the larynx was separated from all surrounding structures with the exception of the laryngeal nerves, a touch of the palate excited the same phenomenon. Under such circumstances the closure of the glottis must have been due to the contraction of its intrinsic muscles and in consequence of a reflex action through the inferior laryngeal nerves.

The Nerve Mechanism of Deglutition.—Deglutition is almost exclusively a reflex act throughout its entire extent, and requires for its inauguration merely a stimulus to some portion of the mucous membrane in the anterior part of the deglutitory canal. The first stage is primarily voluntary, but from inattention to the process may become secondarily reflex. The origin and course of the afferent nerves, stimulation of which excite reflexly the movements of the pharynx and esophagus, however, are practically unknown. In the rabbit deglutition can be excited by stimulating the anterior central part of the soft palate; in man it has not yet been possible to locate an area stimulation of which will give rise to a reflex deglutitory act. Though electric stimulation of the superior laryngeal nerve will cause reflex deglutitory movements, it is obvious that the terminals of this nerve cannot be the source of the natural afferent impulses. Stimulation of the glosso-pharyngeal nerve causes an inhibition of the movements.

The center from which emanate nerve impulses which excite the various muscles to action has been located experimentally in the medulla oblongata just above the alæ cinereæ. The efferent nerves comprise branches of the facial, hypoglossal, motor filaments of the third division of the fifth nerve, motor filaments of the glosso-pharyngeal and vagus nerves derived in all probability directly from the medulla oblongata. Inasmuch as the different mechanisms of this reflex, act not only in a coördinate but sequential manner, it would appear as if the deglutition center sent out, in response to the nerve impulses coming from a single peripheral area, a series of nerve impulses successively to successive portions of the canal, through the groups of nerve-cells corresponding to the origins of the efferent nerves. That this orderly and progressive peristalsis usually observed is due to a sequence of changes in the central nerve system is shown by the fact, that if the esophagus is divided or a ring of it excised, the extremity in connection with the stomach will exhibit a well-marked peristalsis after a short interval, when an act of deglutition is excited in the customary manner. The efferent nerve-fibers, which stimulate the esophageal muscles to action are contained in the trunk of the vagi nerves for after their division the peristalsis is abolished.

In addition to this primary reflex mechanism, the esophagus appears to possess a secondary reflex mechanism consisting of a series of reflex arcs, whose afferent and efferent paths are found in the trunk of the vagus and both connected with successive portions of the esophagus. The first mechanism is temporarily suspended during deep anesthesia while the second persists. (Meltzer.)

Though the peristalsis of the esophagus is excited by nerve impulses coming through the vagus nerves and is abolished by their division, Cannon has shown by means of the Röntgen rays that this effect for the lower portion of the esophagus, at least in the cat and monkey, is of a temporary duration only, lasting from one to several days, after which a peristalsis again develops with sufficient vigor to force food through the cardiac orifice into the stomach. The muscle coat of this portion of the esophagus is composed of non-striated muscle-fibers, is supplied with a myenteric nerve plexus and resembles lower portions of the alimentary canal. It is capable of developing a peristalsis merely in response to the pressure of food within and independent of extrinsic nerves.

GASTRIC DIGESTION

After the food has passed through the esophagus it is received by the stomach, where it is retained for a variable length of time, during which important changes are induced in its physical and chemic composition. The disintegration of the food inaugurated by mastication and insalivation is still further carried on in the stomach by the solvent action of the acid fluid there present, until the entire mass is reduced to a liquid or semi-liquid condition.

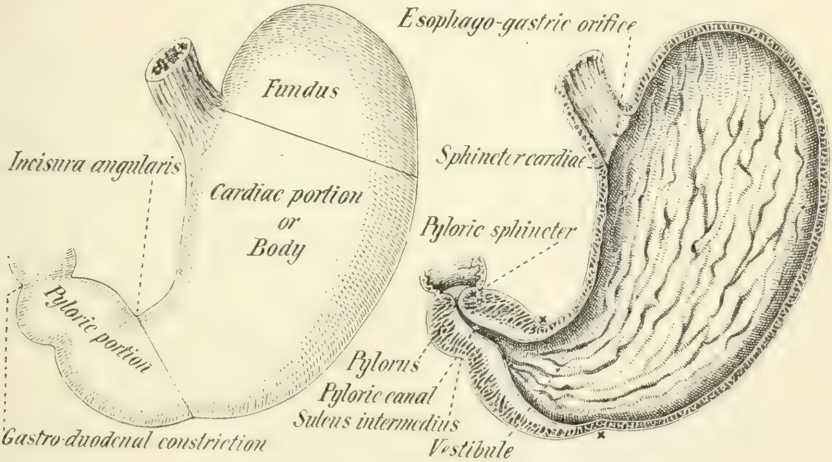

FIG. 71.—ANATOMIC FEATURES OF THE STOMACH.

The Stomach.—The stomach is the dilated and highly specialized portion of the alimentary canal intervening between the esophagus and small intestine. When moderately distended with food, it is somewhat conical or pyriform in shape and slightly curved on itself. It is situated obliquely and in some individuals almost vertically in the upper part of the abdominal cavity, extending from the left hypochondrium to the right of the epigastrium. The dimensions and capacity of the stomach undergo considerable periodic variation according to the extent to which it is distended by food. In the average condition it measures in its long diameter from 25 to 35 centimeters, in its vertical diameter at the cardia 15 centimeters, in its antero-posterior diameter from 11 to 12 centimeters. The capacity of the stomach varies from 1500 to 1700 c.c. In the empty condition its walls are contracted and partly in contact, and the entire organ is drawn up into the upper part of the abdominal cavity. The stomach being a contractile and distensible organ adapts itself to varying amounts of food and hence continually varies in size. The opening through which the food passes into the stomach is known as the esophago-gastric or the cardiac orifice. The opening through which it passes into the intestine is known as pylorus, the pyloric, or gastro-duodenal orifice, indicated on the outer surface by a slight constriction known as the gastro-duodenal constriction. Between these two orifices, the stomach, along its upper border, presents a curve and along its lower border a much larger curve, known as the lesser and greater curvatures respectively. Along the lesser curvature there is a slight indentation due to a change in direction of the right end of the stomach, known as the *incisura angularis*. If this indentation is connected by a line with a point or angle almost opposite on the greater curvature the stomach will be divided into a *pyloric portion* to the right and a *cardiac portion* to the left. If a line be drawn transversely across the stomach from the esophago-gastric or cardiac orifice to the greater curvature, the cardiac portion will be subdivided into the *fundus*, to the extreme left, and the cardiac portion proper or the body included between the fundus and the pyloric portion.

If a vertical section of the stomach is made, it will be observed that the walls are extremely thin to the left but gradually increase in thickness in passing toward the pyloric orifice. The cavity of the pyloric portion, is, when the stomach is empty, subdivided into a *vestibule* and a *pyloric canal* which latter is said to begin at a point opposite the *sulcus intermedius*, and to extend to the pyloric orifice. The pyloric canal is narrow and cylindric and measures from 2.5 to 3.5 centimeters. The vestibule and pyloric canal when distended with food form a tubular region which has been termed the antrum or the gastric canal.

The Walls of the Stomach.—The walls of the stomach are formed by four distinct coats united by areolar tissue and named, from without inward, as the serous, muscle, submucous, and mucous.

The *external* or *serous coat* is thin and transparent and formed by a reduplication of the general peritoneal membrane.

The *middle* or *muscle coat* consists of three layers of non-striated muscle-fibers, named from their direction the longitudinal, circular, and oblique. The longitudinal fibers are most abundant along the lesser curvature and are a continuation of those of the esophagus; over the remainder of the stomach they are thinly scattered, but toward the pyloric orifice they are more numerous and form a tolerably thick layer which becomes continuous with the fibers of the small intestine. The circular fibers form a complete layer encircling the entire organ, with the exception, perhaps, of a portion of the fundus. The fibers of this coat cross the longitudinal fibers at right angles. At the lower end of the esophagus and surrounding the cardia the circular muscle-fibers form a true sphincter which is known as the *sphincter cardiæ*. At the junction of the pyloric and cardiac regions, x–x, Fig. 71, the circular fibers form a well-defined bundle—the transverse band—which was supposed to contract periodically during digestion and thus partially divide the stomach into two portions, the portion to the right of which was termed the *antrum*, and hence this transverse band has been termed the *sphincter antri pylorici*. This function, however, has been questioned.

In the pyloric region the circular fibers are more closely arranged, forming thick well-defined rings termed the *antral muscles*. At the pyloric opening the circular fibers are crowded together and form a distinct muscle band known as the *sphincter pylori* which projects for some distance into the interior of the canal. It has been stated by Rüdinger that the inner fibers of the longitudinal coat become connected with this circular band and constitute a distinct muscle, the *dilatator pylori*. The oblique fibers are most distinct over the cardiac portion of the stomach, but extend from left to right as far as the junction of the middle and last thirds of the stomach. They are continuations of the circular fibers of the esophagus.

The *submucous coat* consists of loose areolar tissue carrying blood-vessels, nerves, and lymphatics. It serves to unite the muscle to the mucous coat. Its inner surface bears a thin layer of muscle tissue, the *muscularis mucosæ*, which supports the mucous membrane.

The *internal* or *mucous coat* is loosely attached to the muscle coat. In the empty and contracted state of the stomach it is thrown into longitudinal folds, or rugæ, which are, however, obliterated when the organ is distended with food. The mucous membrane in adult life is smooth and velvety in appearance, gray in color, and covered with a layer of mucus. Its average thickness is about one millimeter. The surface of the membrane is covered with a layer of columnar epithelial cells. In passing from the cardiac toward and into the pyloric region the mucous membrane becomes thicker and forms the inner wall of the vestibule and pyloric canal. It finally becomes continuous with the mucous membrane of the intestine. At the pyloric orifice there is a circular involution of the mucous membrane which is known as the *pyloric valve*. This is strengthened by fibrous tissue and embraced by the sphincter muscle previously described.

Gastric Glands.—The surface of the mucous membrane when examined with a low magnifying power presents throughout innumerable depressions, polygonal in shape and separated by slightly elevated ridges. At the bottom of these spaces are to be seen small orifices, which are the mouths of the glands embedded in the mucous membrane. A vertical section of the gastric walls shows not only the position and the appearance of the glands, but the relation of the various tissues which enter into the formation of these walls. An examination of the mucous membrane in different regions of the stomach reveals the presence of two distinct types of glands, which from their situation are termed cardiac, and pyloric, which differ not only in histologic structure, but also in function. Both types extend through the entire thickness of the mucosa.

The *cardiac* glands are formed by an involution of the basement membrane of the mucosa and lined by epithelial cells. Each gland may be said to consist of a short duct, or neck, and a body, or fundus (Fig. 72). The latter portion is wavy or tortuous and frequently subdivided into as many as four distinct and separate tubules. The duct is lined by columnar epithelial cells similar to that covering the surface of the mucosa. The lumen of the gland is bordered by epithelial cells, cuboid in shape, and consisting of a granular protoplasm containing a distinct spherical nucleus. These cells are generally spoken of as the *chief* or *central* cells. In addition to the chief cells, the cardiac glands contain a second variety of cell, which is of a larger size, of a triangular or oval shape, and consisting of a finely granular protoplasm. From their situation in and just beneath the gland wall they have been termed *parietal* or *border* cells. Each parietal cell appears to be surrounded and penetrated by a system of passages which open into the lumen of the gland by means of a delicate cleft or canaliculus (Fig. 73). Glands with these histologic features are most abundant in the middle zone of the stomach.

The *pyloric glands* are also formed by an involution of the mucous membrane and lined by epithelial cells (Fig. 74). The ducts are much longer than the ducts of the cardiac glands. At its extremity each duct becomes branched, giving rise to a number, from 2 to 10, of short tubes, each of which has a large lumen and communicates with the duct by a narrow short neck. The ducts are lined throughout by columnar epithelium. According to Mall, the total number of openings on the surface of the mucous membrane of the dog's stomach is somewhat over 1,000,000, and the total number of blind tubes opposite the muscularis mucosæ exceeds 16,500,000. According to Sappey, the surface of the mucous membrane of the human stomach presents over 5,000,000 orifices of gastric glands.

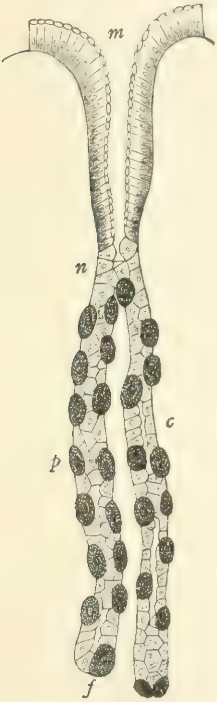

Fig. 72.—Cardiac Gland. *m* Mouth of the duct; *n*, neck; *f*. fundus; *c*, central cells; *p*, parietal cells. (*Landois and Stirling*.)

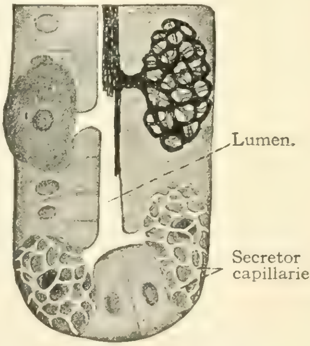

Fig. 73.—Section of Cardiac Gland of Mouse. Left upper half drawn after an alcohol preparation, right upper half after a Golgi preparation. The entire lower portion is a diagrammatic combination of both preparations. (*Stöhr*.)

Blood-vessels and Nerves.—The blood-vessels of the stomach after entering the mucosa break up into a number of branches which are distributed to the muscle and mucous coats. The branches to the latter soon form a capillary network with oblong meshes which not only surround the tubules but form a network just beneath the surface of the mucosa. Veins gradually arise from the capillaries which empty into the larger veins of the mucosa. The glands are also supported by processes of smooth musclefibers passing up from the muscularis mucosæ.

The nerve elements are partly intrinsic and partly extrinsic. The intrinsic nerve elements consist of two nerve plexuses, one which lies between the muscle coats, another which lies between the muscle and the mucous coats. They have been named after their discoverers, Auerbach's and Meissner's plexuses respectively. Each plexus consists of microscopic ganglia and nerve processes which interlace with one another to form a very complicated network. The nerve processes are distributed mainly to muscle-fibers. As these plexuses are associated with a large part of the alimentary canal they together have been termed the *myenteric plexus*. The extrinsic nerves, which associate the central nerve system with the gastric structures are the vagus and the great splanchnic. The vagus nerve, through its efferent nerve-fibers is in physiologic relation with muscle-fibers and gland-cells, through the intermediation of ganglionic cells. The great splanchnic through its efferent nerve-fibers is in physiologic relation with the muscle-fibers and blood-vessels through the intermediation of the post-ganglionic fibers derived from the cells of the semilunar ganglion.

Gastric Fistulæ.—The general process of digestion, as it takes place in the stomach, has been studied in human beings and animals with a fistula in the walls of the stomach and abdomen, the result either of accident, of necessary surgical or of experimental procedures.

The earliest observations on gastric digestion were made by Dr. Beaumont on Alexis St. Martin, who, as the result of a gunshot wound, was left with a permanent fistulous opening into the fundus of the stomach. This opening two years after the accident was about two and a half inches in circumference and usually closed from within by a fold of mucous membrane which prevented the escape of the food. This valve could be readily displaced by the finger and the interior of the stomach exposed to view. After the complete recovery of St. Martin, Dr. Beaumont during the years between 1825 and 1831 at intervals made numerous experiments on the nature of gastric digestion. As the result of an admirable series of investigations it was established that the digestion of the food is largely a chemic act, due to the presence of an acid fluid secreted by the mucous membrane; that this fluid is secreted most abundantly after the introduction of food into the stomach; that different articles of food possess varying degrees of digestibility; that the duration of digestion varies according to the nature of the food, exercise, mental states, etc., and that the process is aided by continuous movements of the muscle walls.

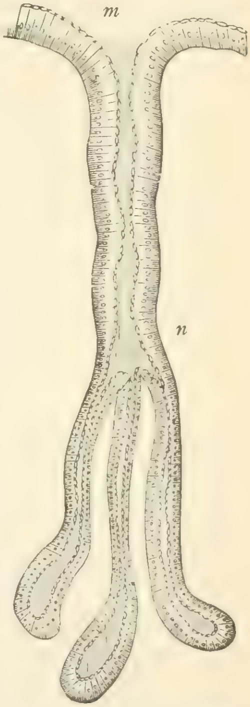

FIG. 74.—PYLORIC GLAND OF THE STOMACH. *m*, Mouth of duct; *n*, neck. (*Landois*.)

Since Dr. Beaumont's time the establishing of a gastric fistula in human beings has been necessitated by pathologic conditions of the esophagus. After recovery these cases offered fair facilities for the study of the process when the food was introduced through the opening. Similar fistulæ have been established in both carnivorous and herbivorous animals with a view of studying the process as it takes place in them. The results obtained in these instances in many respects corroborate those obtained by Dr. Beaumont, though many new facts, unobserved by him, have been brought to light.

Much additional information as to the mode of secretion and the characteristics of the gastric juice has been obtained, since the introduction of two new procedures by Pavlov. The first consists in establishing a gastric fistula and subsequently dividing the esophagus in the neck, and then so adjusting the divided ends that they heal separately into an angle of the skin incision. The second procedure consists in forming a diverticulum or pouch out of the cardiac end of the stomach which opens on the surface of the abdomen but is separated from the rest of the stomach by a thin septum formed of two layers of mucous membrane. (Fig. 75.) The serous and muscle-coats of this pouch are in direct continuity with the large stomach and all possess the same vascular and nerve connections. Because of this fact this miniature stomach, about one-tenth the size of the natural stomach, exhibits the same phenomena, so far as the secretion of the gastric juice is concerned, as the large stomach does. The phenomena which are observed in it may be taken as an indication as to the phenomena which are taking place in the natural stomach.

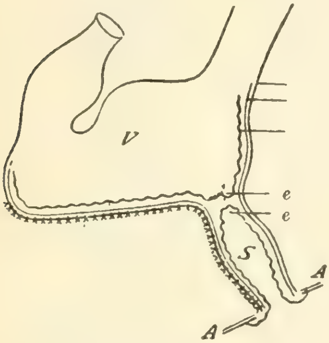

Fig. 75.—Diagram Showing the Relation of the Natural Stomach to the Miniature Stomach or Pouch made According to the Procedure Devised by Pavlov. *V*. The natural stomach. *S*. The miniature stomach. *e*, *e*. The septum formed by the mucous membrane. *A*, *A*. The abdominal walls.

By the first procedure it is possible to feed an animal with different kinds of food and to observe the effects of psychic states on the secretion of gastric juice. As the swallowed food is discharged from the lower end of the divided esophagus the appetite continues, and hence the animal will eat for several hours. By the second procedure it is possible to collect gastric juice from the miniature stomach and to study the effects on its quantity and quality produced by psychic states, mastication, different articles of food, and by the process of digestion itself as it goes on in the large stomach. In both instances the juice is obtained free from admixture with saliva or food.

Gastric Juice.—The gastric juice obtained from the human stomach free from mucus and other impurities is a clear, colorless fluid with a constant acid reaction, a slightly saline and acid taste, and a specific gravity varying from 1.002 to 1.005. The juice obtained from the dog's stomach possesses essentially the same characteristics, though its acidity as well as its specific gravity are slightly greater. When kept from atmospheric influences, it resists putrefactive change for a long period of time, undergoes no apparent change in composition, and loses none of its digestive power. It will also prevent and even arrest putrefactive change in organic matter. The chemic composition of the gastric juice has never been satisfactorily determined, owing to the fact that the secretion as obtained from fistulous openings has not been absolutely normal. It may however be said to consist of water, organic matter, hydrochloric acid and various inorganic salts. The quantitative composition of the juice varies somewhat in different animals.

The organic matter present in gastric juice is a mixture of mucin and a protein, products of the metabolic activity of the epithelial cells on the surface of the mucous membrane and of the chief or central cells of the gastric glands respectively. Associated with the protein material are two possibly three ferment or enzyme bodies, termed pepsin, rennin and lipase. As is the case with other enzymes, their true chemic nature is practically unknown.

Pepsin.—Pepsin, though present in gastric juice, is not present as such in the chief cells of the glands, but is derived from a zymogen, propepsin or pepsinogen, when the latter is treated with hydrochloric acid. This antecedent compound is related to the granules observed in and produced by the cell protoplasm during the period of rest. Though pepsin is largely produced by the central cells of the cardiac glands, it is also produced, though in less amount, by the cells of the pyloric glands. Pepsin is the chief proteolytic or proteoclastic agent of the gastric juice and exerts its influence most energetically in the presence of hydrochloric acid and at a temperature of about 40°C. Other acids—*e.g.*, phosphoric, nitric, lactic, etc.—are also capable of exciting it to activity, though with less intensity.

Rennin.—Rennin or pexin is present in the gastric juice not only of man and all of the mammalia, but also of birds and even fish. In its origin from a zymogen substance; in its relation to an acid medium and an optimum temperature it bears a close resemblance to pepsin. Its specific action is the coagulation of milk, a condition due to a transformation of soluble caseinogen into a solid flaky body, casein.

Lipase.—Lipase, an enzyme found in pancreatic juice, has also been shown to be present in gastric juice, the specific function of which appears to be the digestion or hydrolysis of finely emulsified fat such as is found in milk.

Hydrochloric Acid.—Hydrochloric acid is the agent which gives to the gastric juice its normal acidity. Though the juice frequently contains lactic, acetic, and even phosphoric acids, it its generally believed that they are the result of fermentation changes occurring in the food, the result of bacterial action. The percentage of hydrochloric acid has been the subject of much discussion. The most recent investigations show that the initial acidity of the freshly secreted human gastric juice is between 0.32 and 0.48 per cent. HCl. This initial acidity is reduced by combination with food, admixture with saliva and gastric mucus, and by regurgitation of alkaline duodenal contents, to 0.15 or 0.2 per cent. HCl, the optimum acidity for the proteolytic activity of pepsin. As observed clinically, following various test meals, the acidity of the gastric contents is seen to rise to a maximum as digestion progresses, after which it falls to the optimum point of about 0.2 per cent. HCl.

The immediate origin of the hydrochloric acid is difficult of explanation. That it is derived, however, primarily from the chlorids of the food and secondarily from the chlorids of the blood-plasma has been established by direct experiment. If all the chlorids be removed from the food and all the chlorids be withdrawn from the animal tissues by the administration of various diuretics—*e.g.*, potassium nitrate—there will be a total disappearance of hydrochloric acid from the stomach. On the addition of sodium or potassium chlorids to the food, there is at once a reappearance of the acid.

As to the nature of the process by which the acid is formed, nothing definite is known. Various theories of a chemic and physical character have been offered, all of which are more or less unsatisfactory. As no hydrochloric acid is found either in the blood or lymph, the most plausible view as to its origin is that which regards it as one of the products of the metabolism of the gland-cells, and more particularly of the parietal or border cells, and which for this reason have been termed acid-producing or *oxyntic* cells. From the chlorids furnished by the blood the chlorin is derived, which, uniting with hydrogen, forms the HCl. The base set free returns to the blood, which in part accounts for its increased alkalinity during digestion as well as the diminished acidity of the urine. The acid thus formed passes through the canaliculi, which penetrate and surround the cells, into the lumen of the gland.

Hydrochloric acid exerts its influence in a variety of ways. It is the main agent in the derivation of pepsin and rennin or pexin from their antecedent zymogen compounds, pepsinogen and pexinogen (Warren); it imparts activity to these ferments; it prevents and even arrests fermentative and putrefactive changes in the food by destroying microörganisms; it softens connective tissue, it dissolves and acidifies the proteins, thus making possible the subsequent action of pepsin.

The inorganic salts of the gastric juice are probably only incidental and play no part in the digestive process.

Mode of Secretion.—The observations of Dr. Beaumont and the experiments of many physiologists have made it certain that the secretion of the gastric juice is intermittent and not continuous, that it is only on the introduction and digestion of the food that the normal amount is poured out. During the intervals of digestive activity the stomach is practically free from all traces of the juice. The mucous membrane is pale and covered with a layer of mucus having an alkaline or neutral reaction. The introduction, however, of small portions of food or irritation with a glass rod causes a change in the appearance of the mucous membrane. At the points of irritation the membrane becomes red and vascular and in a few minutes small drops of a secretion make their appearance; these coalesce and run down the sides of the stomach.

The statements of Beaumont and many subsequent investigators that the secretion thus obtained is gastric juice have been apparently disproved by Pavlov, who asserts that it is only an alkaline mucous the function of which is protective in character. According to this investigator, mechanic stimulation is incapable of exciting the secretion. The results of modern methods of investigation make it apparent that the production and discharge of the secretion is the result of the action of two different stimuli, a primary and a secondary.

The *primary* stimulus to gastric secretion, according to Pavlov, is a psychic state induced, on the one hand, by the sight or the odor of food especially if the animal is hungry and the food appetizing; and on the other hand by the mastication of food which is agreeable to the animal. Thus when a dog was tempted by the sight of food, the secretion made its appearance at the end of six minutes and during the time of the experiment, which lasted for an hour and a half, 80 cubic centimeters of the juice were obtained. This is known as *psychic* or *appetite* juice. The character of a psychic state, however, greatly influences the amount of the juice secreted. Agreeable emotions increase, depressing emotions inhibit it. Again when a dog with a divided esophagus and a gastric fistula was subjected to sham feeding, mastication continued for five or six hours during which time 700 cubic centimeters of juice were obtained from the stomach. Similar results have been obtained in human beings with an occluded esophagus and a gastric fistula. It is evident from these facts that the secretion of gastric juice is favorably influenced by the sight and odor of appetizing food, by exhilarating emotional states and thorough mastication.

As a result of the psychic states induced by the sight and odor of food and of the taste of food during mastication, nerve impulses not only descend from the brain but are also transmitted from the mouth through afferent nerves, to some central mechanism; and that from this mechanism, nerve impulses must in turn be discharged to be transmitted through efferent nerve-fibers which are distributed to the epithelium of the gastric glands. Experimental investigations render it probable that the central mechanism is located in the medulla oblongata and that the efferent path for the secretor fibers lies in the trunk of the vagus nerve. Though this nerve has been the subject of much experimentation, the results which have been obtained have not been uniform. The investigations of Pavlov seem to be the most reliable. He found that after division of the nerve, secretion was arrested, and that stimulation of the peripheral ends with induced electric currents at the rate of one or two per second, caused after a latent period of several minutes' duration a flow of gastric juice. Coincidently with the development of the psychic secretion there is a dilatation of the gastric blood-vessels and an increase in the supply of blood to the gastric glands. Whether this is due to the action of vaso-dilatator fibers or to an inhibition of the action of vaso-constrictor fibers is uncertain.

Though the secretion of the gastric juice can be initiated by these means, the amount secreted is but small compared with the quantity secreted after digestion has begun. Then it is that the blood-vessels dilate to their full capacity and furnish for several hours the requisite materials for the production of the juice on a relatively large scale. That some factor is active in keeping up the secretion in the stomach, is apparent from the increase in the quantity and the change in the quality of the juice secreted by the miniature stomach.

The *secondary* stimulus to the gastric secretion is in all probability chemic in character and developed in the stomach or in its walls during digestive activity, inasmuch as the secretion takes place independent of nerve influences and after division of all afferent and efferent nerves that pass from and to the stomach. On the assumption that this factor might be developed in the walls of the stomach itself, Edkins conducted a series of experiments, the results of which lead to the inference that there is developed in the mucous membrane of the pyloric region, by the action of certain articles of food, *e.g.*, dextrin, meat broths, soups, etc., or by the first products of digestive activity, a chemic agent, which is absorbed by the blood and is carried to the glands throughout the stomach and which, on reaching the glands, stimulates their cells in a specific manner. For this reason it has been called the *gastric hormone*[1] or the *gastric secretin.* Whatever the agent or the mechanism may be, there is not only an increase in the quantity but a change in the quality of the juice in accordance with the character of the food; in other words, there is an adaptation of the juice to the kind of food to be digested. Thus the protein of bread causes a secretion of five times more pepsin than the same amount of the protein of milk, while the protein of meat causes a secretion of 25 per cent. more pepsin than milk. Meat extract and bouillon have a very stimulating effect on the quantity of juice produced, while alkalies have an inhibitor effect.

Histologic Changes in the Gastric Cells during Secretion.—During the periods of rest and secretor activity the cells of the gastric glands undergo changes in histologic structure which are believed to be connected with the production of the enzymes, pepsin and rennin, and the acid. In the resting period the protoplasm of the chief or central cells of the cardiac glands becomes crowded with large and well-defined granules, which during the period of secretory activity largely disappear, so much so that only the luminal border of the cell is occupied by them, the outer border being clear and hyaline in appearance. The parietal cells during rest are large and finely granular, but after secretion they are smaller in size though still granular.

The cells of the pyloric glands, though containing granules, do not show any marked difference between the resting and active conditions. According to some observers they contain pepsinogen; according to others, mucin. The epithelial cells lining the ducts of the pylorus and cardiac glands, if not identical with the epithelial cells on the surface of the mucous membrane, pass by transitional forms into them. Among these cells are found many goblet cells which secrete a portion of the mucin found in the stomach and gastric juice. In the period of rest the protoplasm of the epithelial cells absorbs and assimilates from the surrounding lymph-spaces material which eventually makes its reappearance as a product of metabolism in the form of granules and hydrochloric acid. With the onset of digestive activity there is a dilatation of the blood-vessels, an increase in the blood-supply, a stimulation through the nerve-supply of the cells, and an output of a fluid to which the name gastric juice is given.

The Physiologic Action of Gastric Juice.—In the study of the physiology of gastric digestion as it takes place under normal conditions it is important to bear in mind that the foods introduced into the stomach are heterogeneous compounds consisting of both nutritive and non-nutritive materials, and that before the former can be digested and utilized for nutritive purposes they must be freed from their combinations with the latter. This is accomplished by the solvent action of the gastric juice, which in virtue of the chemic activity of its constituents on proteins, gradually disintegrates the food and reduces it to the liquid or semiliquid condition.

The nature of this change and the respective influence which the acid and pepsin exert can be studied with almost any form of protein. A most convenient form, however, is fibrin obtained from blood by whipping and thoroughly freed from corpuscles by washing under a stream of water. The chemic features of proteins, as well as the typical forms contained in the different articles of food, have been considered in connection with the chemic composition of the body and the composition of foods (see pages 15 and 119). For purposes of experimentation artificial gastric juice may be employed. This is as effective as the normal secretion and in no essential respect differs from it. A glycerin extract of the mucous membrane acidulated with 0.2 per cent. hydrochloric acid is probably the best.

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[1] A hormone (from ὁρμαω, "I excite") may be defined as an agent of known or unknown composition which is secreted by some one organ, is discharged into and carried by the blood stream to some correlated organ near or remote, on the functional activities of which it exerts an excitator or stimulating influence. (See Chapter on Internal Secretion.)

If the small pieces of fibrin be suspended in clear gastric juice and kept at a temperature of 104°F. (40°C.) for an hour or two, they will be dissolved and will entirely disappear, giving rise to a slightly opalescent mixture. In the early stages of the process the fibrin becomes swollen and transparent and partly dissolved. If at this time the solution be carefully neutralized, the dissolved portion can be regained in the form of acid fibrin—a fact which indicates that the first effect of the gastric juice is the acidification of the protein. This having been accomplished, the pepsin becomes operative, and in a varying length of time transforms the acid-protein into a new form of protein, termed peptone which differs from all other forms of protein in being soluble in both acids and alkalies and non-coagulable by heat. In the transformation of acid-protein into peptone it is possible to isolate by the addition of magnesium sulphate and ammonium sulphate intermediate bodies to which the term *proteoses* has been given, and which differ somewhat in their solubility. The proteoses are termed, from the order in which they make their appearance, primary and secondary. The primary proteoses are precipitated by magnesium sulphate, the secondary by ammonium sulphate. This supposed change produced by gastric juice is represented by the following scheme:

Protein—Acid-protein—Proteose—Proteose—Peptone
(Primary) (Secondary)

From the fact that when peptones are subjected to the prolonged action of pancreatic juice there arise compounds such as leucin, tyrosin, aspartic acid, arginin, etc., it was believed that two kinds of peptones were formed out of a simple protein one of which succumbed to the destructive action of pancreatic juice, while the other resisted it; for this reason the latter was termed *anti-* and the former *hemi-peptone.* The two were included under the term *ampho-peptone.* It is generally admitted now, however, that there is but one kind of peptone formed from any given protein, which under the influence of pancreatic, and intestinal juice as well, is reduced by hydrolysis, through successive stages to amino-acids or perhaps only to the antecedent stage, in which two or more amino-acids yet remain united forming substances known as peptids.

Nearly all forms of protein are in a similar manner transformed into peptones by gastric juice. Beyond this stage, however, there does not seem to be any further change, peptones apparently being the final products of gastric digestion. The intimate nature of this change is practically unknown, but there are reasons for thinking that it is a process of hydration, attended by cleavage, with increasing solubility of the resulting products.

Characters of Peptones.—The peptones resulting from the digestion of different proteins, though resembling each other in many respects, yet possess different chemic characteristics, as shown by their reaction to various chemic reagents. Though having some resemblance to the proteins from which they are derived, they are to be distinguished from them by the following general characteristics:

1. They are not coagulable either by heat or by nitric acid.
2. They are soluble in water, either hot or cold, and in acid and alkaline solutions.
3. They are diffusible, passing through animal membranes with great rapidity. It has been demonstrated that peptones diffuse about twelve times as rapidly as the proteins from which they are derived.

From the foregoing facts it may be inferred that in the digestion of proteins there is a progressive diminution in the size of the molecules through a series of hydrolytic changes. The molecules of the proteins, which from various causes are coagulated, are transformed into smaller molecules which are non-coagulable, soluble, and diffusible.

On liquid fat and hydrated starch gastric juice has no appreciable action. It has apparently been demonstrated, however, that when fat in the *emulsified* state, the state in which it exists in milk, is introduced into the stomach it undergoes a cleavage into fat acids and glycerin, in a manner similar to that which fat undergoes in the intestine under the action of pancreatic juice, as will be stated in a future paragraph. This presupposes the existence of a ferment to which the name *lipase* has been given. Though the action of saliva on starch is interfered with and even checked by a small percentage of hydrochloric acid it is certain from the results of recent experiments, that starch digestion continues for from twenty minutes to a half hour or longer, for the reason that the acid as fast as it is secreted combines with the proteins and is thus rendered inoperative and for the reason also that the food is largely retained in the extreme fundic end of the stomach where the gastric juice is not abundant. After the above-mentioned period, free acid makes its appearance when salivary digestion ceases.

Notwithstanding the fact that dilute solutions of hydrochloric acid (0.3 per cent.) will promptly invert cane-sugar to dextrose and levulose, and that gastric juice will accomplish the same result in test-tubes, there is no strong evidence for the belief that the inversion of cane-sugar takes place to any marked extent in the stomach under normal conditions.

Action of Gastric Juice on Foods.—The action of gastric juice on proteins affords a key to its action in the reduction of foods to the liquid or semiliquid condition. It is evident that it will be most active in the digestion of food consisting largely of protein materials, such as meat, eggs, milk, etc. Meat is disintegrated first by the conversion of the proteins of the connective tissue, which have been more or less gelatinized by cooking, into peptones. The sarcolemma of the muscle-fibers which have been thus separated is in a similar manner attacked and converted into peptones. The true muscle or sarcous substance, consisting largely of myosin, undergoes a corresponding change. If the quantity of meat be not too large and the gastric juice be secreted in proper amount, it is possible that all the meat will be digested in the stomach. It is quite probable, however, that this is not the case and that a portion of the semidigested meat passes into the intestine, where its final solution is effected.

The white of egg, especially when slightly boiled, is much more readily digested than when raw or firmly coagulated by prolonged boiling. In either condition, however, the supporting tissue is dissolved and peptonized, after which the native albumin undergoes the same change. The yolk of the egg consists largely of fat held in suspension by a protein substance, vitellin, which is also capable of transformation into peptone.

Adipose tissue is similarly reduced. The protein of the connective tissue and of the fat vesicles is dissolved and peptonized and the fat-drops set free.

Milk undergoes a peculiar change in composition before its chief protein constituent, caseinogen, can be transformed into peptone. The caseinogen in the presence of calcium salts is always in the soluble state. When acted on by the gastric juice, the caseinogen undergoes a chemic change by reason of which it combines with calcium salts and is then transformed into a solid compound casein. This change is due to the presence and activity of the enzyme, *rennin*. The necessity for this change in the process of digestion, however, is not apparent. The coagulated casein presents itself in the form of a flocculent curd, which is finer in human than in cow's milk, and hence more easily digestible. After its production, the casein is acidified by the hydrochloric acid and then converted by the pepsin into peptone.

Vegetables, though consisting of a woody or cellulose framework, undergo a partial disintegration in the stomach. When they are boiled and disintegrated by the teeth, the gastric juice is enabled to penetrate the framework and dissolve and peptonize the various protein constituents. As a general rule, the vegetable proteins are more difficult of digestion than the animal proteins.

Duration of Gastric Digestion.—The length of time the food remains in the stomach and the relative digestibility of different articles of food were carefully studied by Dr. Beaumont on St. Martin, and though the results obtained by him may not be absolutely correct, viewed in the light of recent knowledge of the digestive process, yet in the main they have been corroborated in various ways. As a result of many observations Dr. Beaumont came to the conclusion that the average length of time an ordinary meal consisting of meat, bread, potatoes, etc., remained in the stomach undergoing digestion was about three and a half hours, the duration of the process, however, being increased when an excessive quantity of food was taken or the quantity and quality of the gastric juice impaired by abnormal conditions of the system. As soon as the food is liquefied by the gastric juice that portion not absorbed by the gastric vessels passes into the intestines, this continuing for two to three hours until the stomach is completely emptied. The relative digestibility of the different foods was also made the subject of many experiments by Dr. Beaumont. After repeating and verifying his observations made under varying conditions, he summed up his results in a table, of which the following is an abstract, in which the mode of preparation and the time required for the digestion of different foods are exhibited:

The time required for the stomach to discharge any given article of food has been shown by Cannon to depend partly on its chemic composition and partly on its capacity for absorbing hydrochloric acid. From an examination of the stomach and duodenum of the cat by means of Röntgen rays and the fluoroscopic screen, after the administration of equal quantities, 25 c.c., of pure protein, fat, and carbohydrate, mixed with 5 grams of bismuth, it became possible to determine the rate at which they left the stomach from the length of the food masses in the duodenum and small intestine as indicated by the shadows on the screen, at intervals of half an hour or longer. The duration of the observations extended over a period of seven hours.

TABLE SHOWING THE DIGESTIBILITY OF VARIOUS ARTICLES OF FOOD

	Hours.	Minutes.		Hours.	Minutes.
Eggs, whipped	1	20	Soup, barley, boiled	1	30
Eggs, soft boiled	3	..	Soup, bean, boiled	3	..
Eggs, hard boiled	3	30	Soup, chicken, boiled	3	..
Oysters, raw	2	55	Soup, mutton, boiled	3	30
Oysters, stewed	3	30	Sausage	3	20
Lamb, broiled	2	30	Green corn, boiled	3	45
Veal, broiled	4	..	Beans, boiled	2	30
Pork, roasted	5	15	Potatoes, roasted	2	30
Beefsteak, broiled	3	..	Potatoes, boiled	3	30
Turkey, roasted	2	25	Cabbage, boiled	4	30
Chicken, boiled	4	..	Turnips, boiled	3	30
Chicken, fricasseed	2	45	Beets, boiled	3	45
Duck, roasted	4	..	Parsnips, boiled	2	30

When a pure protein, *e.g.*, boiled beef free from fat, boiled haddock, or the white meat of fowls is administered, foods which not only excite the flow of gastric juice but readily absorb hydrochloric acid, the pylorus remains closed for some time, scarcely any protein leaving the stomach during the first half hour. Shortly after this when free hydrochloric acid makes its appearance, the signal for the relaxation of the sphincter, the pylorus opens from time to time and the passage of the protein into the duodenum begins and gradually increases in rapidity until the maximum speed is attained, about two hours after ingestion; from this time on, the speed of discharge gradually diminishes until the end of the observation period.

When fat, *e.g.*, beef, mutton, or pork fat, is administered, they remain in the stomach for some time and when they begin to leave, the rate of discharge is so slow that they are digested and absorbed almost as fast as discharged and hence seldom accumulate in the small intestine. These compounds delay the secretion of gastric juice and therefore free hydrochloric acid, the presence of which appears to be necessary for the relaxation of the pyloric sphincter.

When carbohydrates, *e.g.*, starch paste, boiled rice, boiled mashed potatoes are administered, their discharge begins shortly after their entrance into the stomach; they pass out rapidly, the velocity of discharge reaching its maximum at the end of two hours, after which the speed declines to the end of the observation period. The reason for the early and rapid discharge is to be found in the fact that while the carbohydrates excite the secretion of gastric juice they do not absorb the hydrochloric acid to any appreciable extent. A combination of equal quantities of protein and carbohydrate varies the rate of discharge of each separately. Thus under these circumstances the carbohydrates are not discharged so rapidly nor are the proteins detained so long as usual; a combination of fat with either protein or carbohydrate delays the time of discharge of both. From these facts it may be inferred that the time any given food remains in the stomach will depend on its chemic composition or the relative amounts of its contained protein, fat, and carbohydrate principles.

Movements of the Stomach.—During the period of gastric digestion the muscle walls of the stomach become the seat of a series of movements, usually described as peristaltic in character, which not only incorporate the gastric juice with the food, but also serve to eject the liquefied portions of the food into the small intestine.

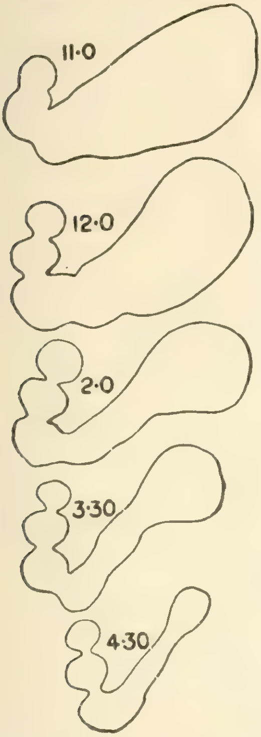


FIG. 76.—SHADOW SKETCHES OF THE OUTLINES OF THE STOMACH OF A CAT IMMEDIATELY AFTER A MEAL (11.0), AND AT VARIOUS INTERVALS AFTERWARD (AT 12.0, AT 2.0, 3.30, 4.30).—(*W. B. Cannon.*)

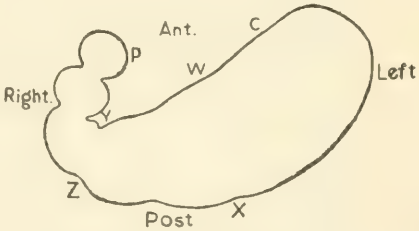


FIG. 77.—The cardiac portion is all that part to the left, as the stomach lies in the body, of *WX*. The cardia is at *C*. The pylorus is at *P*, and the pyloric portion is the part between *P* and *WX*. This has two divisions: the antrum, between *P* and *YZ*, and the pre-antral part, between *WX* and *YZ*. The lesser curvature is on the top of the outline between *C* and *P*, and the greater curvature between the same points along the lower border.—(*Amer. Jour. of Physiology, Cannon.*)

The movements of the human stomach as described by Beaumont, as well as the movements of the dog's stomach as stated by different observers are not in agreement in all respects, and are, moreover, open to question for the reason that they were not observed under strictly physiologic conditions. The more recent investigations of Cannon have thrown new light on this subject. By means of the Röntgen rays he has been enabled to study the movements in the living animal and under normal conditions. The animal (the cat) was fed with bread and milk, to which was added subnitrate of bismuth. This substance, being opaque, rendered the movements of the stomach walls visible on the fluorescent screen. With paper placed over the screen it was possible to sketch the change in shape that the stomach undergoes at different periods of the digestive act. The results of these investigations will be referred to in following paragraphs.

As a result of many methods of investigation it has become apparent that the activities of different portions of the stomach, whereby food is admitted into it, retained there, triturated and mixed with the gastric juice and finally discharged into the duodenum, are due (1) to causes resident in the stomach walls and the stomach contents and (2) to nerve impulses descending from the central nerve system through the vagi and splanchnic nerves.

At the end of a digestive period the walls of the stomach contract and almost obliterate its cavity. The sphincter cardiac and sphincter pylori are also contracted and the orifices they surround are more or less tightly closed.

The Movements of the Sphincter Cardiæ.—The *sphincter cardiæ* muscle surrounding the esophago-gastric orifice is always, under normal conditions, tonically contracted and the orifice closed. This contraction is partly due to inherent causes as shown by the fact that it persists for from 24 hours to several days after division of all nerves distributed to it. The contraction may be so pronounced as to offer considerable resistance not only to the passage of food but even to the introduction of a sound into the stomach. (Cannon.) That the normal contraction is under the influence of the central nerve system is shown by the effects which follow division and stimulation of the peripheral end of the vagus. If it is stimulated with *weak* induced currents, the contraction of the sphincter is somewhat inhibited and the orifice enlarged; if it is stimulated with *strong* currents the contraction is markedly increased and the orifice diminished. Apparently there are in the vagus two sets of efferent nerve-fibers, one of which *inhibits* while the other *augments* the contraction, and corresponding to the nerves there must be in the medulla oblongata two centers from which they arise, an augmentor and an inhibitor.

Observation has also shown that at the beginning of each act of deglutition, there is an inhibition of the sphincter muscle, and if the acts follow each other in quick succession, the inhibition and relaxation are increased. (Meltzer.) With the passage of food into the stomach the tonic contraction again supervenes. These effects also follow stimulation of the glossopharyngeal nerve. Whether the sphincter inhibition is the result of an inhibition of the center which maintains the tonus, or a stimulation of an inhibitor center, is uncertain.

Though the tonus of the sphincter cardiæ is capable of being inhibited and augmented by the central nerve system, the most frequent cause under physiological conditions for an augmentation of the tonus, is the presence of hydrochloric acid on the gastric side of the cardia. In the early stages of digestion when the percentage of the acid is below the normal, the orifice frequently opens and food is regurgitated for a short distance into the esophagus. The ascent of the food far into the esophagus is prevented by a contraction and peristalsis of its muscle walls, by which the food is returned to the stomach. As the free acid accumulates the sphincter tightly closes the orifice. As this takes place after division of the nerves passing to this region of the esophagus the inference is that the contraction of the sphincter is brought about through the intermediation of a local reflex nerve mechanism in the walls of the esophagus.

It has recently been reported by Cannon that a similar inhibition or relaxation of the musculature of the cardiac end of the stomach is occasioned by each act of deglutition and that it continues and increases if the acts follow each other in quick succession. As the bolus descends the esophagus and before it reaches its termination there is a relaxation of the musculature of the cardiac end, a fall of intragastric pressure, an enlargement of the stomach capacity and hence a readier receptivity of the bolus. That this inhibition is caused by impulses descending the vagus is shown by the effects which follow a moderate stimulation of the vagus nerve and by the fact that it does not take place if the vagus nerves are divided. To this inhibition and enlargement of the cardiac end of the stomach the term *receptive relaxation* has been given.

The investigations of Cannon previously referred to, show that not only the sphincter cadiæ, but other portions of the stomach walls exhibit different forms of activity which for convenience of description are separately described by him as follows:

1. *The Movements of the Pyloric Portion.*—The movements of this region of the stomach were first studied and sketched by means of the Röntgen rays by Cannon. Some of the changes in shape due to these movements are shown in Fig. 76. Within five minutes after a cat has finished a meal of bread there is visible near the duodenal end of the antrum or vestibule a slight annular contraction which moves peristaltically to the pyloric orifice; this is followed by several waves recurring at regular intervals. Two or three minutes after the first movement is seen, very slight constrictions appear near the middle of the stomach, and, pressing deeper into the greater curvature, course slowly toward the pyloric end. As new regions enter into constriction, the fibers just previously contracted become relaxed, so that there is a true moving wave, with a trough between two crests. When a wave swings round the bend in the pyloric part, the indentation made by it deepens; and as digestion goes on the antrum or vestibule elongates and the constrictions running over it grow stronger, but, until the stomach is nearly empty, they do not entirely divide the cavity. After the pyloric region has lengthened, a wave takes about thirty-six seconds to move from the middle of the stomach to the pyloric orifice. At all periods of digestion the waves recur at intervals of almost exactly ten seconds. It results from this rhythm that when one wave is just beginning several others are already running in order before it. Between the rings of constriction the stomach is bulged out, as shown in the various outlines in Fig. 77.

2. *The Movements of the Sphincter Pylori.*—During the first ten or fifteen minutes after the introduction of food the pyloric orifice is more or less tightly closed. After this period it opens at irregular intervals to permit the passage of liquefied food which is ejected by peristaltic waves for a distance of two or three centimeters into the duodenum. The frequency with which the pyloric orifice opens depends apparently on the degree to which the food is softened. When the food is hard, the orifice is closed more tightly and remains closed a longer period than when it is soft.

The physiologic cause for the relaxation or inhibition of the sphincter pylori appears to be the presence of free acid at the pylorus; its contraction, the presence of free acid in the duodenum. With the neutralization of the acid in the duodenum, its influence on the sphincter muscle is weakened, after which the muscle again becomes susceptible to the inhibitor influence of the acid within the stomach. It is probably for this reason that carbohydrates, which do not absorb the acid, are discharged from the stomach early; that the proteins, which postpone the appearance of free acid, are retained longer and that fats, which check the secretion of gastric juice are discharged slowly (Cannon). It should be emphasized, however, that the relaxation and contraction of the pyloric sphincter, due to the action of free acid on the gastric and duodenal sides, respectively, can take place independently of the central nerve system, and through the intermediation of a local reflex nerve mechanism, the myenteric plexus, in the walls of the pylorus.

This explanation of the opening of the pylorus is believed by its advocates to supersede a former view, yet widely held, however, that the pylorus remains open until closed reflexly from the duodenum by the passage into it of acid, coarse food particles or other irritants from the stomach. When these irritants are neutralized or removed, the pylorus relaxes, to be closed again by another duodenal reflex. This intermittent opening and closing continues until the stomach empties. Recent investigations apparently suggest this interpretation of the mechanism to be the one that obtains for the human pylorus. In these experiments the stomach was found to empty more quickly when its contents were of a weak alkaline reaction than when acid was present in the gastric contents.

If the pylorus is more or less open during the early stages of digestion it is easier to understand how the intestinal juices can be regurgitated into the stomach, as appears to be experimentally proven by the investigations of Boldyreff, Spencer and his co-workers with the result of neutralizing the superfluous acidity of the gastric juice. The initial high acidity of this fluid, viz.: 0.32 to 0.48 causes, on its passage into the duodenum, a secretion of pancreatic juice and bile and the development of an anti-peristaltic wave or rhythmic pulsations which drives these alkaline fluids into the stomach until the acidity is brought down to that point where the juice is no longer irritating to the duodenal mucous membrane.

3. *The Movements of the Cardiac Portion.*—As digestion proceeds, the prevestibular or cardiac portion of the stomach elongates and assumes the shape of a tube, which becomes the seat also of peristaltic constriction waves. As a result, some of the food is gradually forced into the pyloric region to succeed that which has been prepared and ejected into the duodenum. As the prevestibular tube is emptied of its contents the longitudinal and circular fibers of the fundus steadily contract and gradually force its contents into the tubular portion. This continues until the fundus is completely emptied. The changes in shape which the cardiac portion undergoes during digestion are represented in Fig. 76. The fundus acts as a reservoir for the food and forces out its contents a little at a time as the vestibular mechanism is ready to receive them. Since peristaltic movements are absent from the fundus portion, the food is not mixed with gastric juice, and therefore salivary digestion can continue for a considerable period. There is no evidence of a circulation of food in the stomach as sometimes described. On the contrary, the movement through the elongated tube is in general a progressive though an oscillating one. As the constriction waves rapidly pass over the food it is advanced toward the pyloric orifice, but as this is closed the food is forced backward through the advancing constricted ring for a variable distance.

The effect of the constriction waves is to mix the food with the gastric juice, triturate and soften it. So soon as this is effected, the pyloric orifice opens, when the advancing constriction wave expels it into the intestine. With its expulsion, room is afforded for an additional quantity of food, and hence there is a general advance of the food mass toward the pylorus.

Though these observations were made on the cat, evidence is accumulating which goes to show that in human beings the walls of the stomach exhibit constriction waves which are similar in all respects to those above described. Evidence of this character has been furnished by experiments conducted in the author's laboratory by Spencer and Meyer.

Fig. 78 is a record of the gastric contractions in man as recorded by the lever of a Marey tambour in connection with a thin rubber sausage-shaped balloon. The balloon was swallowed in the collapsed state and then inflated under a pressure of about eight millimeters of mercury. During the experiment, which lasted from one to an hour and a half, the subject was placed in the recumbent position and frequently fell asleep. The abdomen was auscultated for sounds of peristalsis in the intestine. The passage of food from the stomach into the duodenum was easily heard and coincided with a fall of intragastric pressure as recorded in the tracing.

The conditions necessary for the development of the gastric peristalsis are (1) a condition of tonicity of the musculature, *i.e.*, a slight degree of contraction whereby the muscle is shortened; (2) intragastric pressure. When these two conditions are mutually adapted the musculature acquires a certain degree of tension whereupon the peristalsis arises. An excess or deficiency of internal pressure as well as a loss of tonicity prevents peristalsis. The peristalsis has no necessary fixed point of origin but arises at that portion of the stomach in which the two factors previously mentioned bear a certain relation one to the other. From their origin the peristaltic waves pass toward the pylorus as a result of increased internal pressure. The necessary degree of the preliminary tonus is imparted to the musculature by nerve impulses descending the vagi. If these nerves are cut, the tonus is impaired and peristalsis fails to develop. After a variable period the neuromuscular mechanism develops a tonus like that given to it by the vagi, after which the usual peristalsis returns. When once the peristalsis is well developed in digestion, division of the vagi has no effect. (Cannon.)

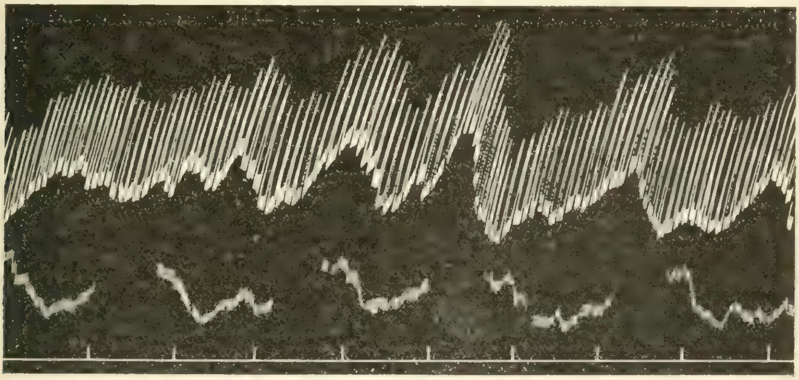


Fig. 78.—Gastric Contractions during Digestion. (Two hours after eating.)

The upper tracing shows respiratory excursions, the variation in the bases of which records the changes in intragastric pressure. The heavier markings at the bases of the respiratory tracings are heart-beats. Time marked in minutes. Analysis of the gastric contractions divides them into long tonus waves of about 60 to 90 seconds duration, superposed upon which are shorter peristaltic waves about 20 seconds in duration.

The lower tracing shows gastric digestive contractions with heart-beats, taken while holding the breath at the end of an expiration. The intervals represent periods of respiration during which the pen was removed from the drum. Were the intervals connected, a regular sequence of gastric tonus waves with peristaltic waves superposed would appear.

The Nerve Mechanism of the Stomach.—In preceding paragraphs it was stated that during the period of gastric digestion the food is retained in the stomach because of the closure of the cardia (the esophago-gastric orifice) and of the pylorus (the gastro-duodenal orifice) both orifices being tightly closed by the tonic contraction of sphincter muscles; that both sphincters relax from time to time, the one to permit the entrance of food into the stomach for further digestion, the other to permit the exit of food into the intestine after its more or less complete digestion, after which in both instances the sphincters again contract and close the orifices; that the fundus muscles are tonically contracted and steadily pressing the food into and through the cardiac region to the vestibule; that the pyloric or vestibular muscles are vigorously active throughout the digestive period, triturating the food, mixing it with gastric juice, and finally driving it through the temporarily open pylorus into the intestine.

These separate but related groups of muscle-fibers, by reason of their physiologic endowments, and possibly by virtue of the presence of local nerve mechanisms, exhibit activities which are independent of the central nerve system. Thus the isolated stomach of the dog and of other animals as well, if kept warm and moist, will exhibit rhythmic movements for a period of time varying from an hour to an hour and a half. Though nerve-cells and nerve-fibers (Auerbach's plexus) are present in the walls of the stomach between the layers of muscle-fibers, it is not believed that they are the immediate sources of the stimulus to the contraction, though they may act as a coördinating mechanism.

Though the activities of the pyloric muscles and of the pyloric sphincter, if not the entire gastric musculature, are due in large measure to conditions referred to in foregoing paragraphs, nevertheless the activities of all portions of the musculature are susceptible to modifications by the central nerve system either in the way of augmentation or inhibition and in response to intragastric stimulation. The nerves more especially concerned in the maintenance and regulation of the gastric tonus and contractions are the vagi and the splanchnics. The *afferent* fibers through which nerve impulses pass to the nerve centers are in all probability contained in the trunk of the vagus nerve; the *efferent* fibers through which nerve impulses from the centers reach the stomach, are contained partly in the trunk of the vagus and partly in the trunk of the splanchnic nerve.

The Vagi.—If the vagus nerves are divided in the neck, there is a loss of muscle tonus though the contractions do not wholly disappear. Stimulation of the peripheral end of one divided vagus is followed by an augmentation in the vigor of the contraction of the antral muscles, an increase in the tone of the fundus muscles, as well as an increase in the contraction of the sphincter pylori and sphincter cardiæ. Though this is the usual result there may be a primary relaxation or inhibition of short duration of one or all of these structures before the augmentation occurs. May states that this was always the case in his experiments. A similar inhibition may be brought about reflexly by stimulation of the central end of a divided vagus. This result will not be produced if the opposite vagus has previously been divided. The vagi, therefore, apparently contain both inhibitor and augmentor nerve-fibers for the gastric musculature.

The Splanchnics.—If the splanchnic nerves are divided and the peripheral end stimulated with induced electric currents there follows an inhibition of the peristalsis and a loss of tone. Morat, however, has observed a primary opposite effect. The splanchnic nerves therefore apparently contain both inhibitor and augmentor fibers for the gastric musculature though the *inhibitor* fibers largely predominate. From these facts it would appear that the gastric muscles receive both inhibitor and augmentor fibers from two different sources.

INTESTINAL DIGESTION

The physical and chemic changes which the food principles undergo in the small intestine, and which collectively constitute intestinal digestion, are complex and probably more important than those taking place in the stomach, for the food is, in this situation, subjected to the solvent action of the pancreatic and intestinal juices, as well as to the action of the bile, each of which exerts a transforming influence on one or more substances and still further prepares them for absorption into the blood.

To rightly appreciate the physiologic actions of the digestive juices poured into the intestine, the nature of the partially digested food as it comes from the stomach must be kept in mind. This consists of water, inorganic salts, acidified proteins, proteoses, peptones, starch, maltose, liquefied fat, saccharose, lactose, dextrose, cellulose, and the indigestible portion of meats, cereals, and fruits. Collectively they are known as chyme. As this acidified mass passes through the duodenum its contained acids excite a secretion and discharge of the intestinal fluids: *e.g.*, pancreatic juice, bile, and intestinal juice. Inasmuch as these fluids are alkaline in reaction they exert a neutralizing and precipitating influence on various constituents of the chyme. As soon as this has taken place, gastric digestion ceases and those chemic changes are inaugurated which eventuate in the transformation of all the remaining undigested nutritive materials into absorbable and assimilable compounds which collectively constitute intestinal digestion.

THE SMALL INTESTINE

The Small Intestine.—This portion of the alimentary canal is a convoluted tube, measuring about seven meters in length and 3.5 cm. in diameter, and extending from the pyloric orifice of the stomach to the beginning of the large intestine.

The Walls of the Small Intestine.—The walls of the intestine consist of four coats: viz., serous, muscle, submucous, and mucous.

The *serous coat* is the most external and is formed by a reflection of the general peritoneal membrane. It is, however, wanting in the duodenal portion.

The *muscle coat*, situated just beneath the former, surrounds the entire intestine. It is composed of non-striated fibers, which are more abundant and better developed in the upper than in the lower portions of the intestine. The muscle coat consists of two layers of fibers: (1) an external or longitudinal, and (2) an internal or circular layer. The longitudinal fibers are most marked at that border of the intestine free from peritoneal attachment, though they form a thin layer all over the intestine. The circular fibers are much more numerous, and completely encircle the intestine throughout its entire extent. It has been demonstrated that at the junction of the ileum and colon, and surrounding the orifice, the *ileo-colic*, common to both, the muscle-fibers are arranged in the form of, and play the part of, a sphincter muscle, which has been termed the *ileo-colic* sphincter. It is usually in a state of tonic contraction and regulates the passage of materials from the small into the large intestine, and possibly also in the reverse direction under special circumstances.

The *submucous coat* consists of areolar tissue and serves to unite the muscle with the mucous coat. A thin layer of muscle-fibers, the *muscularis mucosæ*, is placed on its inner surface.

The *mucous coat* is soft and velvety in appearance and covered by a single layer of columnar epithelium. Its entire surface is covered with small conical projections termed villi. Throughout its entire extent, with the exception of the lower portion of the ileum and the duodenum, the mucous membrane presents a series of transverse folds—the valvulæ conniventes, or valves of Kirkring. These folds vary from one-fourth to half an inch in width and extend one-half to two-thirds of the distance around the interior of the bowel. Each valve consists of two layers of the mucous membrane permanently united by fibrous tissue. It is believed that the valves retard to some extent the passage of the food through the intestine and present a greater surface for absorption.

Blood-vessels, Nerves, and Lymphatics.—The blood-vessels of the small intestine, which are very numerous, are derived mainly from the superior mesenteric artery. After penetrating the intestinal walls the smaller vessels ramify in the submucous coat and send branches to the muscle and mucous coats, supplying all their structures with blood. After circulating through the capillary vessels the blood is returned by small veins which subsequently unite to form the superior mesenteric vein, which, uniting with the splenic and gastric veins, forms the portal vein. The nerve elements in the intestinal wall consist of two plexuses, one (Auerbach's) lying between the muscle coats, the other (Meissner's) lying in the submucous coat. To this nerve net, composed of nerve cells and nerve processes, found in connection with the muscle coats of the stomach, of the small and of the large intestine as well, the term *myenteric plexus* has been given. The lymphatics, which originate in the mucous and muscle coats, are very abundant. They unite to form those vessels seen in the mesentery and empty into the thoracic duct.

Intestinal Glands.—The gland apparatus of the intestine by which the intestinal juice is secreted consists of the duodenal (Brunner's) and the intestinal (Lieberkühn's) glands.

The *duodenal glands* are situated beneath the mucous membrane and open by a short wide duct on its free surface. They are racemose glands lined by nucleated epithelium. The secretion of these glands is clear, slightly viscid, and alkaline. Its chemic composition and functions are unknown.

The *intestinal glands* or follicles are distributed throughout the entire mucous membrane in enormous numbers. They are formed mainly by an inversion of the mucous membrane and hence open on its free surface. Each tubule consists of a thin basement membrane lined by a layer of spheric epithelial cells, some of which undergo distention by mucin and become converted into mucous or goblet cells. The epithelial secreting cells consist of granular protoplasm containing a well-defined nucleus. The intestinal follicles constitute the apparatus which secretes the chief portion of the intestinal juice.

The surface of the mucous membrane presents throughout its entire extent fine fillform or conical processes termed villi. The structure and function of the villi will be considered in connection with the absorption of food materials.

The pancreas and liver are developed, during embryonic life, from the walls of the intestine and are anatomically and physiologically associated with it.

PANCREAS

The Pancreas.—This gland is long, narrow and flattened and is situated deep in the abdominal cavity, lying just behind the stomach. It measures from fifteen to twenty centimeters in length, six in breadth, and two and a half in thickness. It is usually divided into a head, body, and tail. The head is directed to the right side and is embraced by the curved portion of the duodenum; the tail is directed to the left side and extends as far as the spleen

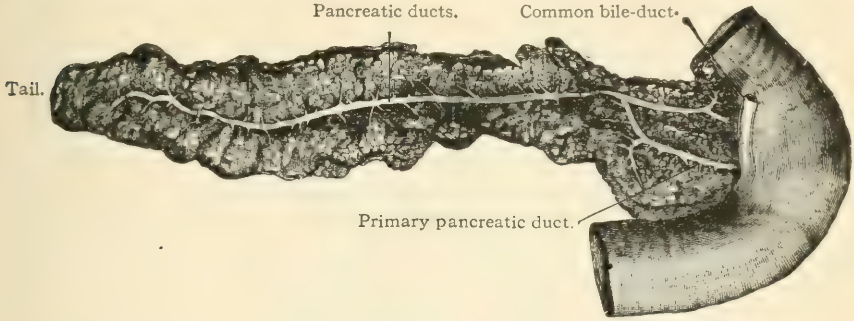


Fig. 79.—Pancreas and Duodenum Removed from the Body and Seen from Behind. The Gland is Cut to Show the Ducts.—(*Landois and Stirling.*)

(Fig. 79). The pancreas communicates with the intestine by means of a duct. This duct commences at the tail and runs transversely through the body of the gland. As it approaches the head of the gland it gradually increases in size until it measures about two or three millimeters in diameter. It then curves downward and forward and opens into the duodenum. In its course through the gland it receives branches which enter it nearly at right angles. The pancreas is richly supplied with blood-vessels and nerves, the latter coming from the solar plexus.

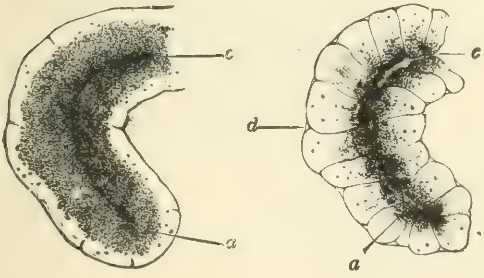


Fig. 80. Fig. 81.

One Saccule of the Pancreas of the Rabbit in Different States of Activity. Fig. 80.—After a period of rest, in which case the outlines of the cells are indistinct and the inner zone—*i. e.*, the part of the cells (*a*) next the lumen (*c*)—is broad and filled with fine granules. Fig. 81.—After the gland has poured out its secretion, when the cell outlines (*d*) are clearer, the granular zone (*a*) is smaller, and the clear outer zone is wider.—(*Kühne and Lea.*)

Histologic Structure.—In its structure the pancreas resembles the salivary glands. It consists of a connective-tissue framework which divides the gland tissue into lobules. Each lobule is composed of a number of acini or alveoli, more or less elongated or tubular in shape. Each acinus gives origin to a small duct which, uniting with adjoining ducts, forms the lobular duct, which becomes tributary to the main duct. The acinus is lined by a layer of cylindric epithelial cells characterized by a difference in structure between their central and peripheral ends (Fig. 80). The central end, that bordering the lumen of the acinus, is dark in appearance and filled with dark granules, while the peripheral end is clear and homogeneous. The relative depth of these two zones varies according to the functional activity of the gland.

During the intervals of digestion the granular layer is very deep and occupies almost the entire cell; after active digestion the granular layer is very narrow, while the clear zone is largely increased in depth (Fig. 81). The blood-vessels of the pancreas are arranged around the acini in a manner similar to that observed in the salivary glands. The ultimate terminations of the nerves in the epithelium are probably by means of the usual end-tufts.

The Islands of Langerhans.—Throughout the body of the pancreas and especially in the outer extremity there are found between and among the acini collections of globular cells arranged in the form of rods or columns, separated from the acini and from one another by layers of connective tissue in which ramify large tortuous capillary blood-vessels. These columnar bodies, seen in cross-section in Fig. 83, have been named, after their discoverer, the islands of Langerhans.

Embryologic investigations have shown that these cells are outgrowths from the primitive acini, to which they remain attached for some time by means of a foot-stalk. This subsequently becomes constricted by the connective tissue and the cells become completely detached. The cells then assume the columnar arrangement, after which vascularization takes place.

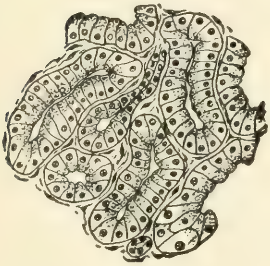


FIG. 82.—SECTION OF HUMAN PANCREAS, INCLUDING SEVERAL ACINI AND TWO DUCTS. THE CELLS PRESENT A CENTRAL GRANULAR AND A PERIPHERAL CLEAR ZONE.—(*Piersol.*)

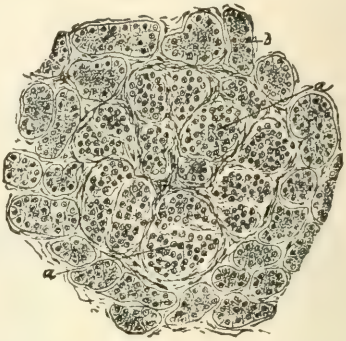


FIG. 83.—SECTION OF HUMAN PANCREAS SHOWING, *a*, *a*, ISLAND OF LANGERHANS, AND *b*, THE USUAL ACINI.—(*Piersol.*)

From the fact that complete extirpation of the pancreas as well as its various diseases is followed by serious disturbances of the carbohydrate metabolism it has been suggested that the islands of Langerhans have a function separate and distinct from that of the glandular portion of the pancreas; that they secrete a specific material which partakes of the nature of an internal secretion which is absorbed by the blood circulating around them and carried to different tissues. The effect on the metabolism of the body which follows extirpation of the pancreas will be referred to in a subsequent chapter.

Pancreatic Juice.—The pancreatic juice may be obtained by introducing a silver cannula, through an opening in the abdominal wall, into the duct, and securing it by a ligature. In a short time the juice flows from the distal end of the cannula, when it can be collected. According to Bernard, normal juice can be obtained only during the first twenty-four hours of the experiment. The juice obtained from a temporary fistula is clear, slightly opalescent, viscid, of a decidedly alkaline reaction, and has a specific gravity (in the dog) of 1.040. When cooled to 0°C., it assumes a gelatinous consistence. At 100°C. it completely coagulates. When obtained from a permanent fistula, the juice is watery and the solid constituents are very much diminished in amount.

The chemic composition of the pancreatic juice of the dog as determined by Schmidt is as follows: water, 900.76; organic matter, 90.44; inorganic salts, 8.80. Of the inorganic salts, sodium carbonate is probably the most essential, as it is this salt which gives to the juice its alkaline reaction.

Human pancreatic juice obtained from a fistula of the duct was found to be clear and limpid, resembling water, alkaline in reaction and with a sp. gr. of 1.007. The total solids of two specimens amounted to about 1.270 and 1.244, grams in 100 grams of the juice. The amount of juice collected varied from 420 c.c. to 884 c.c. daily.

Mode of Secretion.—The secretion of the juice is, in the rabbit and dog at least, almost continuous during a period of twenty-four hours after a single average meal, though the rate of flow varies considerably during this period. Shortly after the food enters the stomach the flow of the pancreatic juice begins, and steadily increases in amount until about the third hour, when it reaches its maximum; after this period the flow diminishes until the sixth hour, when it again increases for about an hour. It then gradually diminishes until it ceases entirely. During the period of secretory activity the blood-supply is very much increased, from a dilatation of the blood-vessels.

The secretion and discharge of the pancreatic juice is associated with the introduction of food into the mouth and stomach and its early passage into the duodenum and is brought about by the action of a primary and a secondary stimulus.

The *primary* stimulus is a psychic state according to Pavlov induced by the sight, odor and taste of food and which leads to the discharge of nerve impulses from nerve-cells in the medulla oblongata and their transmission by efferent nerves in the trunk of the vagus nerve, to the cells of the acini. It is probable that the impressions made by the food on the terminal filaments of the afferent fibers in the vagus nerve develop nerve impulses which, when transmitted to the medulla, occasion the discharge of nerve impulses that not only excite the secretion but increase the blood-supply as well. The vaso-motor nerve impulses reach the blood-vessel supplied to the gland, by way of the great splanchnic nerve and the post-ganglionic fibers from the semilunar ganglion. That the vagus nerve contains secretor fibers for the pancreas has been established by Pavlov. This investigator states indeed that the vagus nerve contains two classes of fibers for the pancreas, secreto-motor and secreto-inhibitor, as well as vaso-dilatator fibers for the blood-vessels, and therefore the effects of stimulation are often contradictory and confused, but if the nerve be divided and time given for the degeneration of the secreto-inhibitor and vaso-dilatator nerves, usually a period of four or five days, then stimulation of the peripheral end of the nerve with induced electric currents is followed after a latent period of two to three minutes by a discharge of the juice. Stimulation of the splanchnic nerve under similar conditions also gives rise to a secretion.

Inasmuch as various agents, such as mineral and organic acids, placed on the duodenal mucous membrane excite the flow, it is quite possible that the passage of the acid contents of the stomach through the duodenum acts as a powerful stimulus to this nerve mechanism. But as the secretion and discharge of the juice is excited by the same conditions after the division of all related nerves, other explanations have been sought for and found in a secondary stimulus discovered by Bayliss and Starling.

The *secondary* stimulus is chemic in character and developed in the glands of the mucous membrane of the duodenum by the action of the acids of the chyme, that is, of the digested foods, coming through the pylorus.

These investigators made the discovery that if an extract of the gland portion of the duodenal mucous membrane, made with hydrochloric acid 0.4 per cent. is injected into the blood it evokes a profuse discharge of pancreatic juice. As hydrochloric acid alone will not produce this effect they assumed that the extract contained an agent that excited or aroused the pancreas to secretor activity and to which therefore they gave the name *secretin.* This agent resists the temperature that usually destroys enzymes and therefore is not regarded as a member of this class of agents. Since hydrochloric acid appears to be necessary to the development of secretin, the further assumption has been made that it is a derivative of a preëxisting compound to which the name *prosecretin* is given. The secretin thus developed is absorbed into the blood and carried eventually to the pancreas and brought into relation with the cells on which it exerts its stimulating action. To an agent of this class Starling has given the name *hormone.*

Histologic Changes in the Cells during Secretor Activity.—Reference has already been made to the fact that the cells lining the acini consist of two zones: an outer one, clear and homogeneous; and an inner one, dark and granular. The position of the nucleus of the cell varies, being at one time in the outer, at another time in the inner, zone. If the pancreas be examined microscopically during the intervals of digestion, it will be observed that the inner zone is broad, highly granular, occupying nearly the entire cell, while the outer zone is narrow and clear. If, however, the gland be examined shortly after a period of active secretion, the reverse conditions will be observed; that is, the inner zone will be narrow, containing relatively few granules, while the outer zone will be clear and wide. This change in the cell has been witnessed in the pancreas of the living animal—rabbit—by Kühne and Lea. They observed that as soon as digestion set in, the granules of the broad inner zone began to pass toward the lumen of the acinus and to disappear gradually as the secretion was poured out, while the outer zone increased in width until almost the entire cell became clear and homogeneous. (See Fig. 81.) After secretion ceased the granules again made their appearance, the result, in all probability, of metabolic activity.

Physiologic Action of Pancreatic Juice.—Experimental investigations have demonstrated the fact that pancreatic juice is the most complex in its physiologic action of all the digestive fluids. By virtue of its contained enzymes, pancreatic juice acts:

1. On *starch.* When normal pancreatic juice or a glycerin extract of the gland is added to a solution of hydrated starch, the latter is speedily

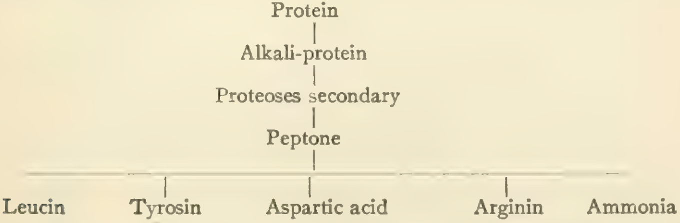
transformed into maltose, passing through the intermediate stage of dextrin. The process is in all respects similar to that observed in the digestion of starch by saliva. Pancreatic juice, however, is more energetic in this respect than saliva. The enzyme which effects this change is termed *amylopsin*. When the starch which escapes salivary digestion passes into the small intestine and mingles with pancreatic juice, it is very promptly converted into maltose by the action or in the presence of this enzyme.

2. On *protein*. When protein compounds are subjected to the action of artificial pancreatic juice, they are transformed into peptones which do not differ in essential respects from those formed by the action of gastric juice. The intermediate stages, however, are believed to be somewhat different. The enzyme which effects this change is termed *trypsin*.

When fibrin, for example, is added to trypsin in a solution rendered alkaline by sodium carbonate, it does not swell and become translucent, as it does when treated with hydrochloric acid and pepsin. On the contrary, it becomes corroded on the surface, fragile, and in a short time undergoes solution. The first product is a compound termed alkali-protein. After solution has taken place, various chemic changes are initiated which eventuate in the production of peptone. The intermediate stages in this process have not been satisfactorily determined. At no time during artificial pancreatic digestion is there any evidence of the presence of the primary proteoses. The secondary proteoses, however, are usually present.

When the proteins which have escaped digestion in the stomach pass into the small intestine and mingle with the pancreatic juice, they are doubtless digested in the course of the intestinal canal, passing through the stages just described. When proteins are artificially digested for a long time there appears a number of compounds such as leucin, tyrosin, aspartic acid, arginin, etc., which are representatives of a group of simple chemical substances known as amino-acids. It would appear that the pancreatic juice had the power under such circumstances of reducing the proteoses or the peptones to their ultimate constituents. Whether this is due to the action of trypsin or to the action of another enzyme *erepsin* is not very clear.

The action of trypsin on proteins in an alkaline medium may be illustrated by the following scheme:



The view that the final stage in the digestion of proteins is the formation of peptones, which in due time are absorbed and synthesized into blood albumin, has been generally abandoned for there is an ever increasing evidence that the final stage is the formation of the nitrogen-holding compounds above mentioned; in other words, that the cleavage of the proteins is far more complete than has heretofore been assumed. Indeed it is now believed that they are reduced, if not to their ultimate constituents, the amino- and diamino-acids, at least to one or more of the different polypeptid stages. Ever since the discovery by Cohnheim of the existence in the intestinal juice of a substance termed by him *erepsin*, which is capable of splitting proteoses and peptones into simple nitrogen-holding compounds, there has been slowly developing the idea that normally during intestinal digestion the proteoses and peptones are reduced by this agent to leucin, tyrosin, histidin, arginin, aspartic acid, ammonia, etc., which in turn are absorbed and transported by the blood direct to the tissues. The discovery by Vernon of erepsin in pancreatic juice lends further support to this view.

3. On *fat*. If pancreatic juice be added to a perfectly neutral fat—olein, palmitin, or stearin—and kept at a temperature of about 100°F. (38°C.), it will at the end of an hour or two be partially decomposed into glycerin and the particular fat acid indicated by the name of the fat used—*e.g.*, oleic, palmitic, stearic. The oil will then exhibit an acid reaction. The reaction is represented in the following formula:

$$\underset{\text{Triolein.}}{C_3H_5(C_{18}H_{33}O_2)_3} + \underset{\text{Water.}}{3H_2O} = \underset{\text{Oleic Acid.}}{3C_{18}H_{34}O_2} + \underset{\text{Glycerin.}}{C_3H_5(OH)_3}$$

If to this acidified oil there be added an alkali, *e.g.*, potassium or sodium carbonate, the latter will at once combine with the fat acid to form a salt known as a soap. The reaction is expressed in the following equation:

$$\overset{\text{Sodium Carbonate.}}{Na_2CO_3} + \overset{\text{Oleic Acid.}}{C_{18}H_{34}O_2} = \overset{\text{Sodium Oleate.}}{2NaC_{18}H_{33}O_2} + \overset{\text{Carbonic Acid.}}{H_2CO_3}$$

Coincident with the formation of the soap, the remaining portion of the neutral oil will undergo division into globules of microscopic size, which are held in suspension in the soap solution, forming what has been termed an *emulsion*, which is white and creamy in appearance. The cause of this minute subdivision of the fat and the necessity for it is unknown. It may be assumed that by virtue of the subdivision a greater surface is exposed to the action of the pancreatic enzyme and the digestion of the fat thereby facilitated. The action of the pancreatic juice may then be said to consist in the cleavage of the neutral fats into fatty acids and glycerin, after which the formation of the soap and the division of the fat takes place spontaneously. The enzyme which produces the cleavage of the neutral fats has been termed *steapsin or lipase*. The extent to which the cleavage of the fat takes place in the intestine has not been definitely determined. There are some who think the amount is relatively small, while others consider that it is large, practically all of the fat undergoing this decomposition, with the formation of soap and glycerin prior to their absorption.

According to Pavlov the relative amounts of the pancreatic enzymes produced, are conditioned by the character and amounts of the food principles consumed. Thus, if chyme contains an excess of either starch, protein, or fat, there is a corresponding increase in the amount of either amylopsin, trypsin, or steapsin produced. The pancreas apparently adapts its activities to the character of the food. Though it is probable that each enzyme is a derivative of a special zymogen, it is positively known that this is the case only with trypsin. This enzyme is a derivative of the zymogen, trypsinogen, the production of which is thought to be the special function of secretin. The pancreatic juice at the moment of its discharge into the intestine does not contain trypsin but trypsinogen. The transformation of the latter into the former is accomplished, according to Pavlov, by a special activating ferment secreted by the epithelium of the small intestine and termed *enterokinase.*[1]

The rapidity with which pancreatic juice in the presence of bile and hydrochloric acid (under conditions such as are present in the duodenum) can develop sufficient fatty acid to form an emulsion was determined by Rachford to be two minutes. The activity of steapsin is thus shown to be very great.

Intestinal Juice.—This fluid is a product of the activities of the cells lining the follicles or glands of Lieberkühn. Owing to its admixture with other secretions and to the profound disturbance of the digestive function caused by the establishment of intestinal fistulæ, this fluid has rarely been obtained in a state of purity or in quantities sufficient for accurate analyses or for experimental purposes. Its physiologic properties and functions are therefore imperfectly known. Various attempts have been made by physiologists, by the employment of different methods, to obtain this secretion. The method usually employed is that of Thiry and Vella. This consists in dividing the intestine at two places, about eight or ten inches apart, restoring the continuity of the intestine, and then uniting the two ends of the resected portion to the edges of two openings in the abdominal walls. The resected portion, being supplied with blood-vessels and nerves, maintains its nutrition and secretes a more or less normal juice.

When obtained from a dog under these circumstances the intestinal juice is watery in consistence, slightly opalescent, light yellow in color, alkaline in reaction, with a specific gravity of 1.010. Chemic analysis reveals the presence of proteins, mucin, and sodium carbonate.

The intestinal juice obtained by Tubbey and Manning from a small portion of the human intestine (ileum) was opalescent, occasionally brownish in color, alkaline, and had a specific gravity of 1.006. On the addition of hydrochloric acid, carbonic acid was given off, showing the presence of carbonates. It contained proteins and mucins.

Physiologic Action of the Intestinal Juice.—The part played by the intestinal juice in the digestive process is yet a subject of discussion, as the results obtained by different observers are in some respects contradictory, due to the fact that animals, as well as human beings, have been the subjects of experimentation. By reason of its contained enzymes the intestinal juice acts:

1. On *Proteoses* and *Peptones.*—Even though the proteins have been reduced by the action of the gastric and pancreatic juices to the stage of proteoses and peptones they are not yet in a condition to be absorbed. The further stage in their digestion appears to be their reduction, as stated in a foregoing paragraph, to amino-acids or their immediate antecedents. This change has been attributed to the action of the intestinal juice or a contained enzyme to which the name *erepsin* was given by its discoverer Cohnheim.

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[1] An activator may be defined as an agent, which secreted by some one organ, is capable of converting an inactive agent, secreted by some correlated organ, near or remote, into an active agent by some chemical interaction. Thus the antecedents of many enzymes, either before or after their discharge by gland cells are inactive and require to be modified in some unknown way before they become functionally active. The term activator is usually applied to inorganic agents, the term kinase to organic agents.

2. On *Compound Sugars.*—Saccharose, maltose and lactose, the three compound sugars, are believed by most observers to be not only non-absorbable, but also non-assimilable and therefore are required to undergo some digestive change before they can be absorbed and assimilated. An extract of the intestinal mucous membrane or the intestinal juice of the dog added to a solution of saccharose will cause it to combine chemically with water after which a cleavage into dextrose and levulose will take place, which together constitute *invert* sugar. The enzyme to which this action is attributed has been termed *invertase* or *saccharase.* Maltose undergoes a similar change. After its combination with water it undergoes a cleavage into two molecules of dextrose. Lactose appears to be unaffected by the pure juice. As it is non-assimilable it has been supposed to undergo conversion into dextrose and galactose while passing through the epithelial cells of the intestinal mucosa. In either case the transformation is brought about by two ferments known respectively as *maltase* and *lactase.*
3. On *Trypsinogen.*—This zymogen when first discharged from the pancreatic duct is inactive and incapable of effecting the necessary digestive changes in the proteins. Shortly after its entrance into the intestine, it becomes quite active and efficient, a change attributed to an agent *entero-kinase* secreted by the mucosa in the upper part of the intestine.

THE LIVER

The Liver.—This highly vascular conglomerate gland is situated in the right hypochondriac region and connected with the intestine by a duct.

Inasmuch as the liver performs several functions related to both secretion and excretion, a consideration of its structure and its various functions will be deferred to a subsequent chapter. In this connection only the bile, its physical properties, chemic composition, and physiologic action in relation to the digestive process, will be considered. This fluid is a product of the secretor activity of the liver cells. As it is poured into the intestine in man and most mammals at a point corresponding to the orifice of the pancreatic duct, and most abundantly at the time the food is passing through the duodenum, it is usually regarded as a digestive fluid possessing an influence favorable if not necessary to the completion of the general digestive process.

Anatomic Relations of the Biliary Passages.—After its formation by the liver cells the bile is conveyed from the liver by the bile capillaries, which unite finally to form the main hepatic duct. This duct emerges from the liver at the transverse fissure. At a distance of about 5 centimeters it is joined by the cystic duct, the distal extremity of which expands into a pear-shaped reservoir, the *gall-bladder* in which the bile is temporarily stored. The duct formed by the union of the hepatic and cystic ducts, the common bile-duct, passes downward and forward for a distance of about 7 centimeters, pierces the walls of the intestine and passes obliquely through its coats for about a centimeter and opens into a small receptacle, the ampulla of Vater. The ampulla in turn opens on a small papilla into the intestine. The walls of the biliary passages are composed of a mucous membrane internally, a fibrous and muscular coat externally. The termination of the common bile-duct is provided with a distinct band of circularly disposed muscle-fibers, which when in action completely close the orifice and prevent the discharge of bile. It may therefore be regarded as a true sphincter muscle, the structure and function of which were first pointed out by Oddi. Small racemose glands are embedded in the mucous membrane of the main ducts.

Physical Properties.—The bile obtained directly from the liver through a cannula inserted into the hepatic duct is always thin and watery, while that obtained from the gall-bladder is more or less viscid from admixture with mucin, the degree of the viscidity depending on the length of time it remains in this reservoir. The specific gravity of human bile varies within normal limits from 1.010 to 1.020. The reaction is invariably alkaline in the human subject when first discharged from the liver, but may become neutral in the gall-bladder. The alkalinity depends on the presence of sodium carbonate and sodium phosphate. When fresh, it is inodorous; but it readily undergoes putrefactive changes, and soon becomes offensive. Its taste is decidedly bitter. When shaken with water, it becomes frothy—a condition which lasts for some time and which is due to the presence of mucin. In ox bile the mucin is replaced by a nucleo-protein.

The color of bile obtained from the hepatic duct is variable, usually a shade between a greenish-yellow and a brownish-red. In different animals the color varies. In the herbivorous animals it is usually green; in the carnivorous animals it is orange or brown. In man it is green or a golden yellow. The colors are due to the presence of pigments. Microscopic examination fails to show the presence of structural elements.

Chemic Composition.—Human bile obtained from an accidental biliary fistula was shown by Jacobson to contain the following ingredients, viz.:

COMPOSITION OF HUMAN BILE

Water	977.40
Sodium glycocholate	9.94
Sodium taurocholate	a trace
Cholesterin	0.54
Free fat	0.10
Sodium palmitate and stearate	1.36
Lecithin	0.04
Organic matter, and pigments bilirubin and biliverdin	2.26
Sodium chlorid	5.45
Potassium chlorid	0.28
Sodium phosphate	1.33
Calcium phosphate	0.37
Sodium carbonate	0.93
	1000.00

In this analysis the solid ingredients constitute 22.6 parts per 1000, of which two-thirds are organic and one-third inorganic. The amount of solid varies according to the animal from which the bile is obtained.

Sodium Glycocholate and Taurocholate.—Of the various ingredients of the bile none are more important than these two salts, usually known as the bile salts. The sodium glycocholate is found most abundantly in the bile of herbivora, the sodium taurocholate in the bile of the carnivora. These salts are compounds of sodium and glycocholic and taurocholic acids. When separated from the sodium, the acids will crystallize in the form of fine acicular needles. Under the influence of hydrolizing agents, such as dilute acids and alkalies, both acids will undergo cleavage into their respective components—*e.g.*, glycocoll and cholic acid, taurine and cholic acid. Glycocoll and taurine are crystallizable nitrogenized compounds known chemically as amido-acetic and amido-isethionic acids respectively.

From the results of the hydrolysis of the bile acids it may be inferred that their formation in the liver cell is the result of an opposite process, viz.: a synthesis of glycocoll and taurin with cholic acid. Glycocoll is an amino-acid and there is much evidence that taurin is a derivative of cystin, another amino-acid, both found in the small intestine. The origin of cholic acid is, however, not so clear. The absorption of the foregoing compounds from the intestine and their transmission to the liver cells by the portal vein furnishes them with the necessary materials for the formation of the bile acids. During the period the bile remains in the biliary passages, the biliary salts hold cholesterin in solution.

There is also good evidence for the view, that after their discharge into the intestine, the bile salts are absorbed, with the exception of a portion destroyed by bacteria, and carried by the portal vein to the liver and again excreted. By this circulation from liver to intestine and from intestine to the liver, the work of the liver cells in the synthesis or secretion of bile acids, is supposed to be reduced to a minimum. It is also probable that a portion of the acids enters the general circulation and influences favorably the general nutrition. It is stated by some investigators that the activities of the liver cells are decidedly increased by the circulation of the bile salts and that they are to be regarded as the natural stimuli to the secretion.

The presence of the bile salts can be demonstrated by the employment of Pettenkofer's test or reaction. It was shown by this investigator that if to a solution of bile salts a small quantity of a 10 per cent. solution of cane-sugar be added and subsequently a small quantity of strong sulphuric acid, a brilliant red color appears which soon passes into a rich purple. To secure the best results in the performance of this test care should be exercised to keep the temperature below 70°C.; the characteristic colors appear to be due to the action of the sulphuric acid on the cane-sugar by which a substance, furfurol, is produced, which in turn reacts with the cholalic acid. This test can be applied to bile directly; thus if to bile in a test-tube cane-sugar be added and the mixture thoroughly shaken, a portion of the bile becomes quite frothy. If now sulphuric acid be carefully added, the red and purple colors present themselves at once in the white froth—an indication that the bile salts are distributed through it.

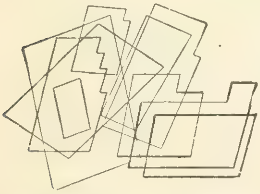

FIG. 84.—CHOLESTERIN CRYSTALS.—(*Landois and Stirling.*)

Cholesterin.—Cholesterin can be obtained directly from bile or better from white gall-stones by the employment of chemic methods described in works on chemistry. When obtained in the pure state it undergoes crystallization when it presents itself in the form of flat rectangular crystals which are soluble in ether and hot alcohol. In the bile it is held in solution by the bile salts. Chemic analysis shows that it is a monatomic unsaturated alcohol with the formula $C_{27}H_{45}OH$. Cholesterin, though a constant constituent of bile, is not confined to this fluid as it has been shown to be a normal constituent of all animal and vegetable cells, though it is particularly abundant in the myelin of nerve-fibers. Though cholesterin has for a long time been regarded merely as one of the products of the katabolism of living material, it has come to be believed that it is necessary to the vitality of tissue cells and especially to the blood cells. Entering into the composition of the surface layer of cells, it prevents the entrance of certain toxins which would have a destructive influence on their structure or composition. In the metabolism of cells it is set free after which it passes into the blood to be secreted by the liver. In the bile it frequently undergoes crystallization and forms one of the forms of gall-stones. In the intestine it is converted into stercorin and discharged in the feces.

Bilirubin, Biliverdin.—These two pigments impart to the bile its red and green colors respectively. Bilirubin is present in the bile of human beings and the carnivora, biliverdin in the bile of the herbivora. As the former pigment readily undergoes oxidation in the gall-bladder, giving rise to the latter pigment, almost any specimen of bile may present any shade of color between red and green. Bilirubin is regarded as a derivative of hematin, one of the cleavage products of hemoglobin, the coloring-matter of the blood. In the liver the hematin combines with water, loses its iron, and is changed to bilirubin. By continuous oxidation there are formed biliverdin, bilicyanin, and choletelin. After their discharge into the intestine the bile pigments are finally reduced to hydrobilirubin or an allied substance, stercobilin, which becomes one of the constituents of the feces. A portion of the latter is absorbed into the blood and ultimately discharged into the urine where it is known as urobilin. The two substances are regarded as identical. An oxidation of the bilirubin can be produced by nitroso-nitric acid. If this agent is added to a thin layer of bile on a porcelain surface, a series of colors will rapidly succeed one another, commencing with green and passing to blue, orange, purple, and yellow. This is the basis of the well-known test for bile pigments suggested by Gmelin.

Lecithin.—Lecithin is regarded, because of its physical properties and chemic composition, as a complex fat. When pure it presents itself generally as a white crystalline powder, though very frequently as a white waxy mass which is soluble in ether and alcohol. Its chemic formula is $C_{44}H_{90}$-NPO_9. Lecithin is widely distributed throughout the body, being found in blood, lymph, red and white corpuscles, nerve-tissue, yolk of egg, semen, milk, and bile. Lecithin has been regarded as one of the decomposition products of nerve-tissue, removed from the blood by the liver and thus becoming one of the constituents of the bile, in which it is held in solution by the bile salts. Lecithin can be readily decomposed by various agents yielding glycophosphoric acid, a fat acid and cholin.

The Mode of Secretion and Discharge of Bile.—The manner in which the bile flows from the liver into the main hepatic ducts, the variations in the rate of its discharge into the intestine, as well as the total quantity secreted daily, have been approximately determined by fistulous openings either in the hepatic ducts or in the gall-bladder. Although the liver presents some physiologic peculiarities, there is no reason to believe that the conditions of secretion therein are different from those in any other secretor organ, or that any other structure than the cell is engaged in this process. As shown by chemic analysis, the bile consists of compounds, some of which, like the bile salts, are formed in the liver cells, out of material furnished by the blood by a true act of secretion, while others, such as cholesterin and lecithin, principles of waste, are merely excreted from the blood to be finally eliminated from the body. The bile is thus a compound of both secretory and excretory principles.

The flow of bile from the liver is continuous but subject to considerable variation during the twenty-four hours. The introduction of food into the stomach at once causes a slight increase in the flow, but it is not until about two hours later that the amount discharged reaches its maximum; after this period it gradually decreases up to the eighth hour, but never entirely ceases. During the intervals of digestion though a small quantity passes into the intestine, the main portion is diverted into the gall-bladder, because of the closure of the common bile-duct by the sphincter muscle near its termination, where it is retained until required for digestive purposes. When acidulated food passes over the surface of the duodenum, there is an increase in the secretion or at least the discharge of bile, and as this takes place after the nerves distributed to the liver are divided, the assumption is that an agent, possibly *secretin*, is developed in the duodenal mucous membrane, which, absorbed into the blood, is ultimately distributed to the liver cells and by which they are excited to activity. At the same time there is excited, through reflex action, a contraction of the muscle walls of the gall-bladder and ducts, a relaxation of the sphincter, and a gush of bile into the intestine, the discharge continuing intermittently until digestion ceases and the intestine is emptied of its contents.

The Influence of the Nerve System.—The storage and the discharge of bile, brought about by the alternate contraction and relaxation of the muscle walls of the gall-bladder and of the sphincter are regulated by the nerve system. As the result of his experiments Doyon concludes, that during the intervals of intestinal digestion the vagus nerve is carrying nerve impulses which on the one hand augment the contraction of the sphincter and inhibit the contraction of the walls of the gall-badder, thus establishing the conditions for the storage of bile; but when intestinal digestion is inaugurated the splanchnic nerve carries nerve impulses which inhibit the sphincter and augment the contraction of the walls of the gall-bladder, thus establishing the condition for the discharge of the bile.

The total quantity of bile secreted daily has been estimated to be from 500 to 800 grams.

Physiologic Action of Bile.—Notwithstanding our knowledge of the complex composition of bile, the quantity discharged daily, and the time and place of its discharge, its exact relation to the digestive process has not been fully determined. No specific action can be attributed to it. It has but a slight, if any, diastatic action on starch. It is without influence on proteins or on fats directly. But indirectly and by virtue of the bile salts it contains, it plays an important part in increasing the action of the pancreatic enzymes. Thus the amylolytic or amyloclastic power of the pancreatic juice is almost doubled and the same is true for its proteoclastic power, while its lipoclastic or fat-splitting power is tripled.

The bile salts also dissolve insoluble soaps which may be formed during digestion and thus favors the digestion of fat. If it be excluded from the intestine there is found in the feces from 22 to 58 per cent. of the ingested fats. At the same time the chyle, instead of presenting the usual white creamy appearance, is thin and slightly yellow. The manner in which the bile promotes fat digestion is yet a subject of investigation. If all the fat is converted into fat acids and glycerin, with the formation of soaps, as seems probable, the action of the bile becomes more apparent from the fact, already stated, that it dissolves and holds in solution the soaps so formed which would be necessary to their absorption by the epithelial cells. This action has been attributed to the presence of the bile salts. As an aid to digestion the bile has been regarded as important, for the reason that its entrance into the intestine is attended by a neutralization and precipitation of the proteins which have not been fully digested and are yet in the stage of acid-albumin. In this way gastric digestion is arrested and the foods are prepared for intestinal digestion.

Though bile possesses no antiseptic properties outside the body, itself undergoing putrefactive changes very rapidly, it has been believed that in the intestine it in some way prevents or retards putrefactive changes in the food. There can be no doubt that if the bile is prevented from entering the intestine there is an increase in the formation of gases and other products which impart to the feces certain characteristics which are indicative of putrefaction. As to the manner in which bile retards this process nothing definite can be stated. It has been supposed to be a stimulant to the peristaltic movements of the intestine, inasmuch as these movements diminish when bile is diverted from the intestine.

Though no definite nor specific action on any of the different classes of food principles can be attributed to the bile, there is abundant evidence to show that its presence in the alimentary canal during digestion is essential to the maintenance of the nutrition of the body. That the bile as a whole, or at least part of its constituents, favorably influences digestion and general nutrition is evident from the phenomena which follow its total exclusion from the intestine, as when the common bile-duct is ligated and a fistula of the gall-bladder is established. The following phenomena were observed in a young dog so prepared by Professor Flint. During the first five days succeeding the operation the abdomen was tumid and there was some rumbling in the bowels. Though the animal ate every day, the discharge of fecal matter became infrequent, the matter passed being grayish in color and highly offensive. After two weeks the alvine discharges took place three and four times daily. For four days the weight remained normal; afterward it began to diminish, and from this time the animal continued to lose strength and weight until its death, thirty-eight days after the operation. Ten days after the operation the appetite, which had been very good, increased, but did not become ravenous until a few days before death. The animal usually ate about a pound and a half of beef-heart daily, but always refused fat. There was an absence at all times of jaundice, fetor of the breath, and falling of the hair. Post-mortem examination showed that the bile-duct was obliterated, and there was no evidence that any bile could have passed into the intestine. The results of this and similar cases go to show that that portion of the bile which is secretory in character is essential to digestion and the nutrition of the body—that, though large quantities of food are consumed, progressive diminution of weight takes place until nearly 40 per cent. of the body is consumed. In some instances the breath becomes fetid and there is a falling of the hair, showing some profound disturbance of the general nutritive process.

The Movements of the Small Intestine.—During the period of intestinal digestion, the walls of the intestine exhibit a series of movements which triturate the food, mix it with the intestinal secretions, gradually transfer it from the upper to the lower portions and promote the absorption of the prepared food materials. The movements of the small intestine have been studied by means of the Röntgen rays by Cannon. The method adopted was to mix with the food subnitrate of bismuth, which being opaque rendered the movements of the intestinal contents and thereby the movements of the intestinal walls visible on the fluorescent screen. There investigations revealed the presence of two forms of activity, one of which is more or less stationary and due to rhythmic contraction of circular muscle-fibers, the other progressive, passing from above downward and due to the contraction of circular and longitudinal muscle-fibers. The former activity, which is by far the more common, results in a division of the intestinal contents into small segments and for this reason was termed by Cannon rhythmic segmentation; the latter activity is the well-known peristaltic wave.

Rhythmic Segmentation.—When the abdominal cavity is investigated by the method above mentioned, it is observed that after the food has passed into the intestine and formed a more or less consistent mass of variable length, bands of circular muscle-fibers, situated at regular distances one from another, begin to contract and divide a mass of food into segments, after which they at once relax to be followed by contraction of other bands in the segments of the intestines overlying the segments of food. The result is again a division of the food into two new segments (Fig. 85). The lower half of each segment then unites with the upper half of the segment of food below to commingle with it and expose new surfaces of the food mass to contact with the actively absorbing mucosa. The continual repetition of this process results in a thorough mixing of the food with the digestive juices. From the manner in which these contractions make their appearance it would seem that the mere presence of a segment of food in the lumen of the intestine is sufficient to excite the overlying fibers to activity.

In certain regions of the intestine rhythmic segmentation may continue for half to three-quarters of an hour without moving the food forward to any marked extent. In the cat the segmentation may proceed at the rate of thirty divisions a minute.

Peristalsis.—After the food has been prepared by the process described in the foregoing paragraph, it is then slowly carried downward by what is known as the vermicular or peristaltic wave. This wave is characterized by a contraction of the circular fibers behind the mass of food and a relaxation of the fibers in advance of it. The result is a movement forward of the food, and as it moves it is followed by a ring of constriction and preceded by a ring of relaxation or inhibition. The rate of movement of the peristaltic wave is usually extremely slow except in the duodenal region where it is quite rapid.

The first of these two movements to make its appearance is the peristaltic which arises at the upper portion of the duodenum from which it sweeps downward with considerable rapidity, carrying with it the food which has been discharged from the stomach and which has accumulated in this region. From the appearance, as shown by Röntgen ray examination, which the extreme upper portion of the duodenum presents, due to its distension by food, it has been designated, the cap or *pilleus ventriculi*.

After the peristaltic wave has advanced the food a variable distance, it disappears and the food comes to rest. By this procedure the incoming food from the stomach is readily accommodated in the duodenal portion of the intestine. With the disappearance of the peristaltic wave, rhythmic segmentation again arises in the portion of the intestine corresponding to the new situation of the segment of food. This in turn is succeeded by another peristaltic wave which advances the food to a more distant region of the intestine. This continues until at the end of gastric digestion a more or less continuous column of food occupies the lumen of the small intestine from the stomach to the ileo-cecal valve.

In addition to this characteristic physiologic movement it has also been observed by different experimenters that the intestine manifests under special circumstances two other forms of moving waves, waves moving downward as well as upward from their point of origin, but without being preceded by an inhibition or relaxation. These waves are therefore not regarded as true peristaltic waves. To avoid confusion, the term *diastalsis* has recently been employed (Cannon) to designate the true peristaltic movement, viz.: progressive contraction preceded by inhibition, and the terms *katastalsis* and *anastalsis* to designate the descending and ascending contractions respectively, that occur without a forerunning inhibition.

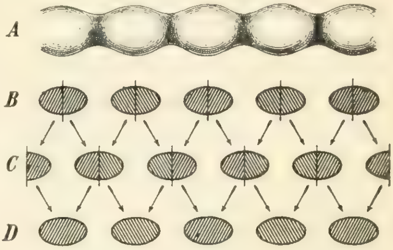

Fig. 85.—The Divisive or Segmenting Movements of the Small Intestine. A, surface of a portion of the intestine, showing six constrictions which divide the contents into five segments, as shown in *B*: as these constrictions pass away new ones come in between them and divide each segment of the contents into two, the adjoining halves of neighboring segments fusing to make the new segments shown in *C*. Repetition of this process results in the condition shown in *D*.—(*Modified, after Hough and Sedgewick, "The Human Mechanism."*)

Rush Peristalsis.—Under conditions that are perhaps not strictly physiologic, a rapid and far-reaching peristalsis is developed which may pass over the intestine, from the duodenum to the cecum without stopping in the course of 15 seconds, in the rabbit, and which has been designated *rush peristalsis*. It is characterized by a wave of constriction preceded by a completely inhibited long section of intestine. The contents of the intestine are carried along with extreme rapidity and vigor. The contractions may be increased by purgative salts, ergot, barium chlorid, etc., the inhibition may be increased by calcium chlorid, magnesium chlorid, etc. A combination of ergot and calcium chlorid develops in the rabbit a pronounced rush peristalsis (Meltzer). This movement appears to be under the control of the central nerve system as it fails to develop after division of the vagus nerves.

Bayliss and Starling state, from observations made on the exposed intestine of a dog, that in addition to the usual peristaltic movement the intestinal coils exhibit a swaying or pendulum movement accompanied by slight waves of contraction which may arise apparently at any point and pass down the intestine. These contractions may occur from ten to twelve times a minute and travel at a rate varying from two to five centimeters a second. In how far this movement represents the normal movement as it takes place under physiologic conditions and as observed by Cannon, remains for further investigations to decide.

The Nerve Mechanism of the Small Intestine.—The causes of these two forms of intestinal activity, rhythmic segmentation and peristalsis, have been the subject of much investigation. Because of the presence of a network or plexus (Auerbach's and Meissner's) of nerve-cells and nerve-fibers in the walls of the intestines and in close relation to the muscle cells, the so-called *myenteric plexus* and because of the fact that the intestines will contract for some time after removal from the body of the animal, it has been difficult to decide whether the contractions are myogenic or neurogenic.

As the rhythmic contractions continue though the peristaltic are abolished by the introduction of nicotin into the blood, an agent which temporarily paralyses peripheral nerve-cells, it was concluded by Bayliss and Starling that the rhythmic contractions are myogenic and that the peristaltic contractions are reflex in character, the coördination being carried out by the local nerve mechanisms and initiated by stimulation of the intestine. This observation has been corroborated by Cannon who has shown that if the myenteric plexus is divided by incisions extending around the intestine, at intervals of 1.5 to 2 cm. for a distance of 45 cm., incisions reaching to the submucous coat, the peristaltic movement is totally abolished though rhythmic segmentation develops as usual and continues for long periods.

As the segmentation activity continues after interruption of the myenteric plexus, the inference is justifiable that it is purely myogenic and is the response to a stimulus within the intestine such as distension by food, when the intestinal wall possesses the requisite degree of tonicity.

Though the orderly and coördinated contractions and relaxations of the muscle coat, which constitutes a peristaltic movement, are mediated by the myenteric plexus, and therefore termed a myenteric reflex, nevertheless the contraction may be augmented or inhibited by the central nerve system through the *vagus* and *splanchnic* nerves respectively.

Stimulation of the vagus is followed by an augmentation of the contraction, though not infrequently there is a primary inhibition of short duration. Stimulation of the splanchnic is followed by a relaxation or inhibition of the contraction, though according to some observers there is at times an opposite effect.

The extent to which the contraction is initiated or augmented by stimulation of the vagus depends upon the extent to which the contraction at the moment is inhibited by the splanchnic. Thus after the splanchnics are divided, stimulation of the vagus causes a much more pronounced contraction than would otherwise be the case; a fact that indicates that the splanchnic nerve-center is in a state of tonus or tonic activity and therefore exerting a constant inhibitor effect on the muscle-fibers. Stimulation of the peripheral end of the divided splanchnic causes an arrest or inhibition of a preëxisting contraction.

The nerve-centers regulating the contraction and relaxation of the muscle walls of the intestine are doubtless excited to activity by nerve impulses transmitted through afferent nerves, probably the vagus, from the mucous surface of the small intestine. These centers are also influenced by nerve impulses descending from the cerebrum, though the route they take is not clearly defined. It is well known that mental states markedly influence the contraction in one direction or another.

It has also been experimentally determined that the introduction of various acids and gases into the intestinal canal is followed by an increase in the contraction. It is probable therefore that the gases, acids, and perhaps other compounds as well, developed by bacterial action also act as excitants to muscle activity.

The Large Intestine.—The large intestine is that portion of the alimentary canal situated between the termination of the ileum and the anus. It varies in length from one and a quarter to one and a half meters, in diameter from three and a half to seven centimeters. It is divided into the cecum, the colon (subdivided into an ascending, transverse, and descending portion, including the sigmoid flexure), and the rectum.

The cecum is situated in the right iliac fossa. It is that dilated portion of the large intestine below the orifice of the small intestine. The posterior and inner wall presents a small opening which leads into a narrow round process about ten centimeters in length—the vermiform appendix. The opening of the small intestine into the cecum is narrow and elongated and bordered by two folds of mucous membrane strengthened by fibrous and muscle-tissue. These folds constitute the so-called ileo-cecal valve. When the cecum is distended the margins of these folds are approximated and effectually prevent the return of material into the small intestine.

The closure of this opening is now attributed to the activity of a sphincter muscle, the *ileo-colic*, the contraction of which is regulated by the nerve system, by way of the splanchnic nerves.

The colon ascends to the under surface of the liver, where it bends at a right angle, forming the hepatic flexure, crosses the abdominal cavity to the spleen, forming the splenic flexure, descends to the left iliac fossa, and bends again. At this point it turns upon itself to form the sigmoid flexure. The rectum is a dilated pouch, situated within the true pelvis. It measures from 15 to 18 centimeters in length. Within three centimeters of its termination at the anus it presents a constriction formed by a circular band of smooth muscle-fibers known as the *internal* sphincter. The margin of the anus is also surrounded by bands of striated muscle-fibers known collectively as the *external* sphincter.

The walls of the large intestine consist of three coats: viz.: serous, muscular, and mucous.

The *serous* is a reflection of the general peritoneal membrane.

The *muscle* is composed of both longitudinal and circular fibers. The longitudinal fibers are collected into three narrow bands which are situated at points equidistant from one another. At the rectum they spread out so as to surround it completely. As the longitudinal bands are shorter than the intestine itself, its surface becomes sacculated, each sac being partially separated from adjoining sacs by narrow constrictions. The circular fibers are arranged in the form of a thin layer over the entire intestine. Between the sacculi, however, they are more closely arranged. The sacculi have been termed *haustra* from their supposed function, that of absorbing or drawing water from the intestinal contents thus imparting to them a certain degree of consistency. In the rectum the circular fibers are well developed, and at a point two or three centimeters above the anus they form, as stated above, the *internal* sphincter.

The *mucous membrane* of the large intestine possesses neither villi nor valvulæ conniventes. It contains a large number of tubules consisting of a basement membrane lined by columnar epithelium. They resemble the follicles of Lieberkühn. The secretion of these glands is thick and viscid and contains a large quantity of mucin.

The Movements of the Large Intestine.—As a result of the actions of saliva, of gastric, intestinal, and pancreatic juice, and of the bile, the food is disintegrated and liquefied. The nutritive principles, protein, starches, sugars, and fats, undergo chemic changes and are transformed into amino-acids and peptids, dextrose, soap and glycerin, fat acids, under which forms they are absorbed. After the more or less complete digestion and absorption of these nutritive substances the residue of the food, comprising the indigestible and undigested matter, passes out of the small intestine into the large intestine and forms a portion of its contents. This residue consists of the hard parts of the cereals, vegetable seeds, cellulose, etc., the quantity and variety of which depend on the nature of the food. These substances, passing into the large intestine along with the excrementitious matter of the bile, become incorporated with the mucous secretions and assist in the formation of the feces.

Under the influence of a peristaltic movement similar to that witnessed in the small intestine, all this excrementitious matter, deprived by absorption of the excess of its contained water and nutritive material, is gradually carried downward to the sigmoid flexure, where it accumulates prior to its extrusion from the body. The effects of the peristaltic waves are to some extent interfered with by *anti-peristaltic* or *anastaltic* waves which, beginning in the transverse colon, run toward and to the cecum. An anti-peristaltic wave occurs in the cat about every fifteen minutes and lasts for about five minutes. The intestinal contents are thereby driven back toward the cecum. The effect is a still further admixture with the secretions and exposure to the absorbing mucosa. There is some evidence also that the anti-peristaltic waves may force some of the liquefied contents through the ileo-colic opening into the small intestine because of the relaxation of the ilio-colic sphincter muscle. It is questionable if this ascending movement is a true peristalsis inasmuch as the advancing contraction is apparently not preceded by an area of inhibition or relaxation. It resembles rather the corresponding movement manifested by the small intestine to which the term *anastalsis* has been given, and is propagated along the muscle coat independently of the myenteric plexus.

In addition to this anastaltic wave, *haustral* contractions have been observed which resemble the segmentation contractions of the small intestines and which promote, it is believed, the absorption or drawing of water from the intestinal contents.

The Function of the Large Intestine.—The large intestine, by reason of its anatomic relation to the small intestine, serves as a receptacle for the temporary storage of the indigestible residue of the food together with certain excretions of the intestinal glands both of which have descended from the small intestine. Inasmuch as the contents of the large intestine, in that portion known as the ascending colon are quite liquid, while the contents in the portion known as the descending colon are more or less solid, it is apparent that an absorption of liquid must take place during the transit from the cecum to the rectum. This is made possible by the retardation of the intestinal contents caused by the antiperistaltic or the anastaltic wave, together with the haustral contractions. Between the two modes of activity different portions of the intestinal contents are exposed to the mucosa and by which the liquids are in large measure absorbed. In the distal portion of the large intestine, the characteristic movement is peristaltic by which the more solid contents are carried to the sigmoid flexure where they accumulate until the desire to evacuate the mass is experienced. By the contraction of the pelvic portion of the descending colon the mass is forced into the rectum from which it is discharged from the body. The function of the large intestine is therefore to receive, to reduce to a proper consistency, to temporarily store and subsequently discharge its contents, consisting of the indigestible residue of the food, together with excretions of intestinal glands which have descended from the small intestine and which constitute in part the feces.

The Nerve Mechanism of the Large Intestine.—The nerve mechanism of the large intestine includes both motor and inhibitor nerves. The motor nerves comprise both pre- and post-ganglionic fibers; the former have their origin in the spinal cord, from which they emerge in the third and fourth sacral nerves and pass by way of the pelvic nerve to the pelvic ganglia around the cells of which their fibers arborize; the latter (post-ganglionic) fibers emerge from the cells of these ganglia and are distributed to circular and longitudinal muscle-fibers of the intestinal wall.

The inhibitor fibers also comprise both pre- and post-ganglionic fibers; the former have their origin in the lumbar region of the spinal cord, from which they emerge in the second to the fifth lumbar nerves; they then pass into and through the sympathetic chain and the inferior splanchnic nerves to the inferior mesenteric ganglion around the cells of which they arborize; the post-ganglionic fibers pass directly to the muscle-fibers of the intestinal wall. Stimulation of the pelvic nerve with induced electric currents causes contraction of the muscle-fibers; stimulation of the hypogastric nerves causes an inhibition of the contraction.

Intestinal Fermentation.—Owing to the favorable conditions in both the small and large intestine for fermentative and putrefactive processes—*e.g.*, heat, moisture, oxygen, and the presence of various microörganisms—some of the food, when consumed in excessive quantity or when acted on by defective secretions, undergoes a series of decomposition changes which are attended by the production of gases and various chemic compounds. Dextrose and maltose are partially reduced to lactic acid; this to butyric acid, carbon dioxid, and hydrogen. Fats are reduced to glycerol and fat acids, the glycerol, according to the organisms present, yields succinic acid, carbon dioxid, and hydrogen. Some of the protein derivatives—the amino-acids—may be reduced to still simpler compounds under the action of bacteria. Lysin, through the loss of a molecule of CO_2, gives rise to cadaverin; ornithin to putrescin; tryptophan yields indol, skatol; tyrosin yields phenol and probably cresol.

Indol.—This compound is of especial interest as it is the antecedent of indican, found in the urine. Though it is in part discharged in the feces, it is in part absorbed into the portal blood and carried direct to the liver where it is oxidized to indoxyl and combined or conjugated with potassium sulphate forming the salt potassium indoxyl sulphate or *indican*, after which it enters the blood, is carried to and eliminated by the kidneys. The presence of this salt in the urine can be demonstrated by adding hydrochloric acid with a small quantity of potassium chlorate; after this is done the indican combines with water and undergoes a cleavage into indoxyl and potassium sulphate; the former then combines with oxygen and gives rise to indigo blue. The extent to which the indican is present is taken as a measure of the extent of intestinal putrefaction.

Skatol.—This compound is also a derivative of the protein molecule, the result of bacterial decomposition. It passes in part into the feces and gives to them the characteristic odor. It is also in part absorbed into the portal blood and carried direct to the liver where it is oxidized to skatoxyl, after which it combines with potassium sulphate to form potassium skatoxyl sulphate after which it enters the blood and is carried to the kidneys to be eliminated in the urine.

Phenol and Cresol.—These compounds, also derivatives of the protein molecule, are absorbed into the portal blood and undergo a similar conjugation. They too are finally eliminated by the kidneys.

The Feces.—The feces is a term applied to the mass of material ejected from the rectum through the anus. They are characterized by consistency, color and odor. The origin and the nature of this material have both a physiologic and a clinic interest.

The consistency varies from day to day from liquid to solid, depending partly on the character of the food, the rapidity with which it is transported through the intestine and hence the extent to which absorption of water in the large intestine takes place. On a meat diet the consistency is firm; on a vegetable diet it is apt to be soft. The amount discharged from day to day on a mixed diet varies from 120 to 170 grams containing from 30 to 42 grams of dry matter. On a meat diet alone the quantity diminishes; on a vegetable diet, especially if the articles of food are rich in cellulose, the quantity will increase considerably beyond the customary amount.

The color on a mixed diet varies from a light yellow to black. The usual brown color is due to the pigment urobilin or stercobilin, a derivative of the pigments of the bile. On a meat diet the color deepens until it becomes quite black due to the presence of sulphid of iron, the result of the union of sulphuretted hydrogen with the iron derived from hematin contained in the meat. On a vegetable diet the color lightens and may become slightly yellow. If the contents of the intestine are carried forward too rapidly, the time may be insufficient for a complete reduction of the bile pigments, hence they appear in the feces imparting to them a green color. If there is an obstruction to the discharge of bile into the intestine the feces may become yellow or clay-colored.

The odor is characteristic and due to the presence of skatol and allied bodies produced by the putrefaction of proteins by bacterial action. Sulphuretted hydrogen also contributes to the odor.

The chemic composition of the feces is complex. They consist of water, mucin, an indigestible residue of food, decomposition products, excretions from the intestinal glands, and inorganic salts. The residue of the food usually consists of the denser portions of the connective tissue of meats and the cellulose of vegetables and cereals. When the latter are eaten in large amounts the cellulose residue is increased and by its mechanic stimulation increases the peristalsis and hastens the transfer of the feces through the intestine. The decomposition products are derived from protein, fat, and carbohydrate food by bacterial action and include skatol, indol, fat acids, soaps, xanthin, ammonia, sulphuretted hydrogen, etc. The excretion from the intestine itself contributes a considerable portion to the fecal mass. The inorganic salts include phosphates of calcium and magnesium together with various sodium and potassium compounds.

Defecation.—Defecation is the final act of the digestive process and consists in the expulsion of the indigestible residue of the food and its associated compounds from the intestine. This act usually takes place in the human being but once in twenty-four hours, as the diet contains but a minimum quantity of indigestible matter. Previous to their expulsion the feces which have accumulated in the sigmoid flexure must pass downward into the rectum. In so doing they develop the sensation which leads to the act of defecation. The descent of the feces is accomplished by the peristaltic contraction of the intestinal wall. Coincident with the passage of the feces into the rectum there is a relaxation of the sphincter muscles and a contraction of the longitudinal and circular muscle-fibers, in consequence of which the feces are expelled. These complex muscle actions are also aided by the voluntary contractions of the diaphragm and abdominal muscles.

Nerve Mechanism of Defecation.—The act of defecation is primarily reflex though somewhat influenced by voluntary efforts. The reflex character of the act is especially noticeable in young children in whom by reason of the imperfect development of the brain there is a lack of volitional control. During the intervals of defecation the anal orifice is tightly closed by the tonic contraction of the internal non-striated sphincter and the external striated sphincter muscles, thus preventing the escape of gases or semi-liquid material. The tonic contraction of both muscles is maintained by the activity of nerve-centers located in the lumbar region of the spinal cord. The circular and longitudinal fibers of the rectum proper are at the same time in a relaxed or inhibited condition, the result of an inhibition, or a want of stimulation, of their governing nerve-center or centers in the lumbar region of the spinal cord. When the desire to evacuate the bowel is experienced, impressions are being made by the feces on the afferent nerve endings in the mucous membrane of the sigmoid flexure and of the rectum. The nerve impulses thus developed are transmitted to the defecation or rectal nerve-centers in the spinal cord and to the cerebrum and influence in one direction or another their activities.

In the young child the arrival of the transmitted impulses in the spinal cord is immediately followed by an inhibition of the sphincter centers and a stimulation of the rectal muscle centers, as a consequence of which, the sphincter muscles relax and the expulsive muscles contract thus discharging the feces.

In the adult if the act of defecation is to be permitted the same mechanism is brought into action. In their expulsive efforts, these latter muscles are assisted by the contraction of the diaphragm, abdominal, and other muscles in response to volitional efforts. After the expulsion of the feces, there is a return to the former condition, namely, a relaxation or inhibition of the rectal muscles and a contraction of the sphincter muscles. If the act of defecation is to be suppressed, the controlling influence of the nerve-center on the contraction of the external sphincter may by an act of volition be strengthened and the action of the reflex mechanism for a while antagonized. The nerve mechanism therefore involves both efferent and afferent nerves as well as nerve centers in the lumbo-sacral region of the spinal cord.

Efferent Nerves.—The *efferent* nerve-fibers for the external sphincter muscle have their origin in the spinal cord from which they pass by way of the third and fourth sacral nerves, the pelvic nerve and the inferior hemorrhoidal nerve directly to the muscle.

The *efferent* nerve-fibers, for the longitudinally and circularly arranged muscle-fibers of the rectum, including the specialized portion, the internal sphincter, have their origin in nerve-cells in the lumbo-sacral region of the spinal cord and pass to their destination by two paths. The fibers in the *first* path leave the spinal cord by way of the second to the fifth lumbar nerves, then pass into and through the sympathetic chain, through the *inferior splanchnics* to the inferior mesenteric ganglion around the cells of which their terminal branches arborize; from the cells of this ganglion new fibers emerge which pass through the *hypogastric nerves* to the muscles. The fibers of the *second* path leave the spinal cord by way of the second to the fourth sacral nerves, then pass into the pelvic or erigens nerve to small ganglia along the sides of the rectum around the cells of which their terminal branches arborize; from the cells of these ganglia new nerve-fibers emerge which pass directly to the muscles. In both paths the nerves coming from the cord are pre-ganglionic, those coming from the ganglia, post-ganglionic.

The central mechanism that excites and coördinates the activities of the rectal muscles is situated in the lumbo-sacral region of the spinal cord and is designated the recto-anal center.

The Afferent Nerves.—The afferent nerve-fibers that excite the central mechanism to activity are contained in the dorsal roots of the spinal nerves. Although the anatomic relations of the various nerves composing this mechanism are fairly well known, their physiologic actions are not clearly defined. The results of experimental methods of investigation are neither uniform nor in accord. The want of accord lies partly in anatomic peculiarities of the animal the subject of the investigation, and partly perhaps in the character of the stimulus employed.

Stimulation of the pelvic nerve causes, in the dog at least, a peristalic contraction of the circular fibers of the rectum. Stimulation of the hypogastric nerve causes an inhibition or relaxation of the circular fibers of the rectum and of the internal sphincter as well. Inasmuch as these two groups of fibers have opposite functions it may be assumed that the nerve centers controlling them, both motor and inhibitor, are double centers and that they can be made to act separately and alternately.

Recalling the events that take place, it may be assumed that peripheral stimulation of the afferent nerves develops nerve impulses which, when transmitted to the cord cause 1, a stimulation of the motor center, a discharge of nerve impulses through the pelvic nerve to the rectal muscles calling forth a contraction; 2, a stimulation of the inhibitor center, a discharge of nerve impulses through the hypogastric nerve to the internal sphincter and perhaps the external sphincter as well, calling forth their relaxation or inhibition. With the discharge of the feces the former condition is re-established. A stimulus, the nature of which is not fully known, causes a stimulation of the inhibitor center for the rectal muscles and a stimulation of the motor center for the sphincters, the nerve impulses reaching the muscles through the hypogastric and pelvic nerves respectively.

CHAPTER XI

ABSORPTION

Absorption is a process by which nutritive material from the tissue spaces, from the serous cavities, from the interior of the lungs and from the mucous surfaces of the body, and waste materials from the tissues are transferred into the blood.

The absorption of nutritive materials from the tissue spaces and from the serous cavities may be regarded as an act of resorption or a return to the blood of nutritive material which has passed across the walls of the capillary blood-vessels in excess of that needed for purposes of nutrition, and which if not returned would lead to an accumulation and the development of edematous conditions; the absorption of oxygen from the lungs is essential to the maintenance of nutritive activity, to the oxidation of foods and the liberation of their energy; the absorption of new nutritive materials from the mucous surfaces of the entire alimentary canal, but more especially from that of the small intestine, materials that have been produced out of the foods by the digestive process, is essential to the maintenance of the quantity and quality of the blood.

The absorption of the products of metabolism, of carbon dioxid, urea and other nitrogen-holding compounds from the tissues into the blood is essential to the continuance of their activities as well as a necessary preliminary to their elimination from the body.

The anatomic mechanisms involved in the absorptive process are, primarily, the *tissue* or *lymph-spaces*, the *blood-* and *lymph-capillaries;* secondarily, the *blood-vessels* (*veins*,) and the *lymph-vessels.*

Tissue or Lymph-spaces.—Everywhere throughout the body, in the connective-tissue system and in the interstices of the several structures of which an organ is composed, are found spaces or clefts of irregular shape and size, determined largely by the structure of the organ in which they are found, which have been termed tissue or lymph-spaces, from the fact that they contain a clear fluid, the lymph. These spaces are devoid for the most part of any endothelial lining, but as they communicate more or less freely one with another, there is a circulation of lymph through them and around the islets of tissue (Fig. 86). In addition to the connective-tissue lymph-spaces, different observers have described special spaces or clefts in organs such as the kidney, liver, spleen, testicle, and in all secreting glands between their basement membrane and the surrounding blood-vessels, all of which contain a greater or less quantity of lymph. Within the brain, spinal cord, bone, and other tissues it has been shown that the smallest blood-vessels and capillaries are bounded and limited by a cylindrical sheath containing lymph, which is known as a perivascular lymph-space. A similar sheath surrounds the smallest nerve-bundles and fibers, enclosing a perineural lymph-space. The large serous cavities of the body, pleural, peritoneal, pericardial, etc., are also to be regarded as lymph-spaces. The surfaces of these cavities, however, are covered with a layer of endothelial cells with sinuous margins. At intervals between these cells are to be found small free openings which have received the name of *stomata*.

The Blood-capillaries.—The blood-capillaries not only permit of a transudation of the liquid nutritive material from the blood across their delicate walls, but are also engaged, if not in the resorption of a portion of this transudate, at least in the absorption of waste products resulting from tissue metabolism.

The Blood-vessels.—The blood-vessels—the venules—that arise from the capillary-vessels gradually converge and unite to form veins which by their union ever increase in size until they terminate in the inferior and superior vena cava, both of which at their terminations communicate with the right side of the heart. The blood containing the waste products absorbed from the tissues, is conducted by these veins to the right side of the heart, thence by the pulmonic artery into the lungs, where the carbon dioxid is eliminated; the blood carrying the remainder of the waste products is then conducted by the pulmonic veins to the left side of the heart by which it is discharged into the arteries and distributed in part to the kidneys, liver, skin and intestine; by these organs the remaining waste products are excreted from the blood.

The Lymph-capillaries.—The lymph-capillaries in which the lymph-vessels proper take their origin are arranged in the form of plexuses of quite irregular shape. In most situations they are intimately interwoven with the blood-vessels, from which they can be readily distinguished by their larger caliber and irregular expansions. The wall of the lymph-capillary is formed by a single layer of endothelial cells with characteristic sinuous outlines. These capillaries anastomose very freely one with another and communicate, on the one hand, with the lymph-spaces and on the other with the lymph-vessels proper. It was formerly believed that the communication of the lymph-capillary with the tissue space was a direct one, the lymph flowing from the latter into the former through an open passage-way. Recent investigation would indicate that this histologic arrangement does not exist but that on the contrary the lymph-capillaries are closed vessels and that the tissue space and the interior of the lymph-capillary are separated one from the other by a thin partition of endothelial cells. As the shape, size, etc., of both lymph-spaces and capillaries are

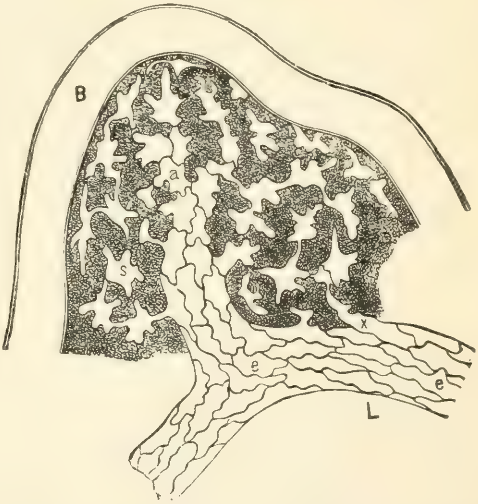

FIG. 86.—ORIGIN OF LYMPH-VESSELS FROM THE CENTRAL TENDON OF THE DIAPHRAGM STAINED WITH NITRATE OF SILVER. *s*. The lymph-spaces and lymph-canals, communicating at *x* with the lymphatics. *a*. Origin of the lymphatics by the confluence of several juice canals. B. Capillary blood-vessels.—(*Landois and Stirling.*)

determined largely by the nature of the tissue in which they are found, it is not always possible to separate one from the other. Their function, however, may be regarded as similar: viz.: the reception and collection of the excess of lymph which has transuded through the walls of the blood-vessels and its transmission onward into the regular lymph-vessels.

Lymph-vessels.—The lymph-vessels constitute a system of minute, delicate, transparent vessels found in nearly all the organs and tissues of the body, and take their origin from the lymph-capillaries and spaces above described. From their origin they gradually converge toward the trunk of the body, and finally empty into the thoracic duct. In their course they anastomose very freely with adjoining vessels. The diameter of a lymph-vessel varies from 1 to 2 mm. After the lymph-vessels have emerged from the lymph-capillaries they acquire three distinct coats, each of which possesses definite histologic features.

The *internal coat* is composed of a delicate lamina of longitudinally disposed elastic fibers covered with a layer of flattened nucleated endothelial cells with wavy outlines.

The *middle coat* consists of white fibrous tissue arranged longitudinally and of non-striated muscle and elastic fibers arranged transversely.

The *external coat* consists of practically the same structures, though the muscle-fibers are longitudinally disposed.

The lymph-vessels are provided with valves which are so numerous and located at such short intervals as to give the vessels a beaded appearance. These valves are arranged in pairs and consist of two semi-lunar folds with their concavities directed toward the larger vessels. They are formed by a reduplication of the lining membrane, which is strengthened by fibrous tissue derived from the middle coat.

Lymph-nodes, or glands.—In their course toward the thoracic duct the lymph-vessels pass through a number of small pisiform bodies termed lymph-nodes or glands. These are exceedingly abundant in some situations, as the cervical, axillary, and inguinal regions, and the abdominal cavity. As the lymph-vessels approach a gland they divide into a number of branches before entering it, known as the afferent vessels. From the opposite side of the gland the lymphatics again emerge as efferent vessels to unite to form larger trunks. A section of a gland shows that it consists of an outer dense cortical and an inner soft pulpy medullary portion. Each gland is covered externally by a dense membrane of fibrous tissue containing in its meshes non-striated muscle-fibers. From the inner surface of this membrane there pass inward septa of connective tissue which, as they converge toward the center of the gland, divide its outer zone into small conical compartments or alveoli. When the septa reach the medullary portion, they subdivide and form bands or cords which interlace in every direction and constitute a loose meshwork the spaces of which communicate with one another and with the alveoli. Within the meshes of this framework the proper gland substance is contained. In the cortical compartments it is moulded into pear-shaped masses; in the medullary meshwork it assumes the form of rounded cords which are connected with one another. In both regions, however, it is separated from the septa by a space termed a *lymph sinus*, through which the lymph flows as it passes through the gland. The lymph sinus is crossed by a network of retiform connective tissue which offers considerable resistance to the passage of the lymph. The gland substance consists also of a framework of retiform connective tissue in the meshes of which large numbers of lymph-corpuscles are contained. The gland substance is separated from the lymph sinus by a dense layer of a reticulum, which, however, does not prevent lymph and even corpuscles from passing through it into the lymph sinus.

The lymph-glands are abundantly supplied with blood-vessels. The arteries enter the gland at the hilum, penetrate into the medullary substance, and terminate in a fine capillary plexus which is supported by the connective tissue. The veins arising from this plexus leave the gland also at the hilum.

The lymph-vessels which enter a gland first ramify in the investing membrane and then open directly into the lymph sinus. The vessels which leave the gland are also in communication with the sinus. After the lymphatics enter the gland they lose their external and middle coats, retaining only the internal or endothelial coat, which lines the inner surface of the lymph sinus. The current of lymph, therefore, is from the afferent vessels through the lymph sinus into the efferent vessels. In addition to this primary current, there is a secondary current flowing from the capillary blood-vessels outward and into the sinus. The lymph flowing through the sinus carries with it large numbers of lymph-corpuscles. It is quite probable that the movement of the lymph through this complicated system of passages is aided by the contraction of the muscle-fibers in the capsule of the gland.

The lymph-corpuscles or lymphocytes originate for the most part in the gland substance of the cortical alveoli. In this situation there are groups of cells, so-called germ centers, which divide very rapidly by mitosis and give rise constantly to groups of young cells which soon find their way into the lymph stream.

The Thoracic Duct.—The thoracic duct is the general trunk of the lymph system, into which the vessels of the lower extremities, of the abdominal organs, of the trunk, of the left arm, and of the left side of the head empty their contents. It is about fifty centimeters in length and four millimeters in diameter. It extends upward from the third lumbar vertebra along the vertebral column to the seventh cervical vertebra, where it empties into the venous system at the *junction of the internal jugular* and *subclavian veins* on the *left* side. The thoracic duct wall has the same general layers as the wall of the lymph-vessel: viz., an internal or endothelial; a middle elastic and muscular; an external or fibrous. It is also provided with numerous valves.

The lymph-vessels of the right side of the head, of the right arm, and a portion of the right side of the trunk terminate in the *right thoracic duct,* which is about 25 to 30 mm. in length and which empties into the venous system at the junction of the internal jugular and subclavian veins on the right side. The general arrangement of the lymphatic system is diagrammatically shown in Fig. 87.

LYMPH

Lymph is the clear fluid found within the tissue spaces and within the lymph-vessels. Inasmuch as there are reasons for the view that lymph varies in composition, as well as in function, in these different regions it will be found conducive to clearness to designate the lymph found in the tissue spaces as *intercellular* lymph, and that found in the lymph-vessels as *intravascular* lymph.

The Physical Properties of Lymph.—Whether obtained from tissue spaces or from lymph-vessels, the lymph presents practically the same physical properties. The lymph obtained from the thoracic duct during the intervals of digestion or from one of the large trunks of the leg is a clear, colorless or slightly opalescent fluid having an alkaline reaction and a specific gravity of 1.020 to 1.040. Examined microscopically it is seen to hold in suspension a large number of corpuscles similar to those seen in the lymph-glands and to the white corpuscles of the blood. Their number has been estimated at about 8000 per cubic millimeter, though this count will vary within wide limits according as the lymph examined has passed through a larger or smaller number of glands. The lymph-corpuscle consists of a small quantity of protoplasm in which is embedded a distinct nucleus. Some of these lymphocytes contain distinct granules, more or less refractive, which impart to the corpuscle a granular appearance. When withdrawn

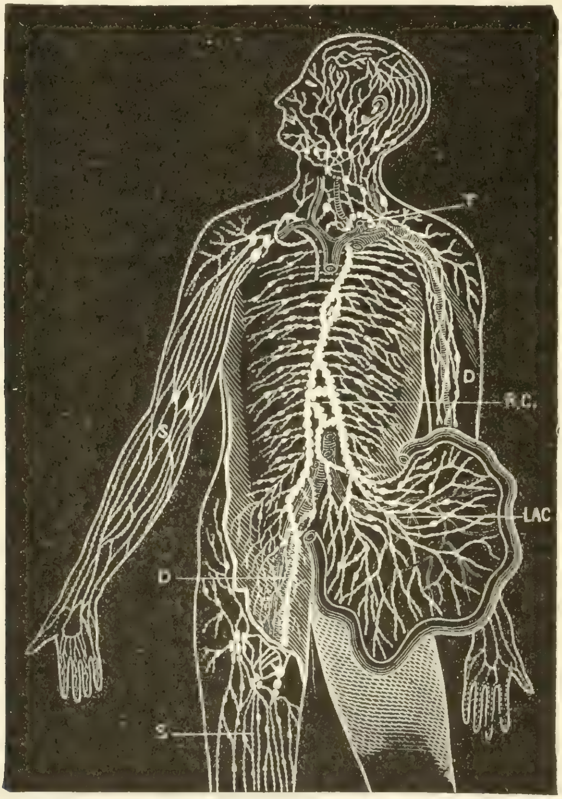

FIG. 87.—DIAGRAM SHOWING THE COURSE OF THE MAIN TRUNKS OF THE ABSORBENT SYSTEM. The lymph-vessel of lower extremities (D) meet the lacteals of intestines (LAC) at the receptaculum chyli (RC), where the thoracic duct begins. The superficial vessels are shown in the diagram on the right arm and leg (S), and the deeper ones on the arm to the left (D). The glands are here and there shown in groups. The small right duct opens into the veins on the right side. The thoracic duct opens into the union of the great veins of the left side of the neck (T).—(*Yeo's "Text-book of Physiology."*)

from the vessels lymph undergoes a spontaneous coagulation, though the coagulum is never as firm as that observed in the coagulation of the blood. The cause of the coagulation is the appearance of fibrin. After a variable length of time the coagulum separates into a liquid and a solid portion, the serum and the clot.

The Chemic Composition of Lymph.—Although the lymph obtained from the tissue spaces, from the lymph-vessels, as well as from the so-called serous cavities has the same general chemic composition, there is reason for the view that it varies in its ultimate composition according as it is derived from one region of the body or from another. The needs of any individual tissue as well as the character of its metabolic products will in all probability change not only its normal composition, but also the relative amounts of its normal constituents.

Chemic analysis has shown that the lymph from the thoracic duct contains from 3.4 to 4.1 per cent. of proteins (serum-albumin, fibrinogen), 0.046 to 0.13 per cent. of substances soluble in ether (probably fat), 0.1 per cent. of sugar, and from 0.8 to 0.9 per cent. of inorganic salts, of which sodium chlorid (0.55 per cent.) and sodium carbonate (0.24 per cent.) are the most abundant (Munk). There are usually in most specimens small quantities of potassium, calcium, and magnesium salts. Fibrinogen is seldom present beyond 0.1 per cent., which will account for the feeble and slow coagulation. Lymph contains both free oxygen and carbon dioxid. Of the former, however, there is but a small percentage; of the latter, about 45 vols. per cent., partially in the free state and partially combined with sodium. Urea is also present in very small amounts. This analysis indicates that lymph resembles blood-plasma in the character of its constituents, though their relative quantities vary considerably. With the exception that it contains no red corpuscles, lymph may be regarded as a diluted blood.

The Production of Lymph.—Though blood is the common reservoir of nutritive material, the latter is not available for nutritive purposes as long as it is confined within the blood-vessels. The capillary wall, thin as it is, and composed of but a single layer of endothelial cells, would be sufficient to prevent its utilization by the tissues, if it were not permeable to the liquid portion of the blood. As this is the case, however, it is found that as the blood flows through the capillary vessels a portion of the blood-plasma passes across the capillary wall and is received into the tissue-spaces, where it comes into intimate contact with the tissue-cells.

The forces concerned in the passage of the constituents of the blood-plasma across the capillary wall have been the subject of much investigation. According to some investigators, diffusion, osmosis, and filtration are sufficient to account for all the phenomena. For a consideration of the phenomena of diffusion, osmosis, and filtration the reader is referred to paragraphs at the end of this chapter. It is assumed that the capillary wall, being an animal membrane, is freely permeable to water and crystalloid bodies generally; less so, however, to colloid bodies, such as the proteins of the blood-plasma; moreover, it is further assumed that the physiologic conditions of the capillary walls are such as not only to permit of the passage of the constituents of the blood into the tissue spaces, but also the passage of the constituents of the intercellular lymph into the blood, according to laws similar at least to those determining the passage of substances through animal membranes as determined experimentally. The force giving rise to filtration is the difference of pressure between that exerted by the blood within the capillary vessels and that exerted by the fluid in the tissue spaces; hence any increase or decrease of this difference of pressure is attended by an increase or decrease in the production of lymph. Thus compression of the veins of a part which interferes with the outflow of blood from the capillaries, or a dilatation of the arterioles which increases the inflow of blood to them will increase the capillary pressure and therefore the production of lymph. The reverse conditions will, of course, diminish the intracapillary pressure and lymph production. Hemorrhages which lower the general blood-pressure may so lower the capillary pressure as not only to stop the flow of lymph to the tissues, but may give rise to a filtration current from the tissues into the blood.

The quantitative composition of the lymph compared with that of the blood indicates that it is produced by diffusion, osmosis, and filtration. In the lymph the concentration of the inorganic salts is practically the same as in the blood; the concentration of the proteins, however, is somewhat less. These facts are in accordance with what is known regarding the diffusibility of both crystalloids and colloids through animal membranes.

According to Heidenhain, the production of lymph is not so much due to intracapillary pressure as it is to the specialized activities of the endothelial cells, activities which indicate that lymph is a secretion the composition of which varies in different situations by virtue of a difference in the molecular structure of the endothelial cells. As is the case with many of the secreting cells of the body, the injection of various substances into the blood apparently increases the activity of the endothelial cells, as shown by an increased lymph production without any appreciable increase of intracapillary pressure. Thus it has been shown that the injection of peptones, albumin, the extract of the muscles of the leech, crab, mussel, etc., is followed by an increase in the amount of lymph discharged from the thoracic duct; the lymph also possesses a high degree of concentration, being rich not only in inorganic but also in organic constituents. The cause of this increase in both the quantity and quality of the lymph is believed to be an increased activity in the secreting power of the endothelial cells. These substances Heidenhain regarded as true lymphagogues.

It has also been shown that after the injection into the blood of sugar, sodium chlorid, sodium sulphate, urea, etc., there is an increase in the flow of lymph from the thoracic duct. The lymph, however, under these circumstances is richer in water than is normally the case. As the blood at the same time increases its percentage of water, it is assumed that the water is extracted from the tissues, by reason of the increased percentage of salts and a higher osmotic pressure. The increased volume of blood raises the intra-capillary blood pressure which in turn gives rise to a greater flow of lymph.

The more recent experiments of Starling indicate that in addition to the difference of pressure between the blood in the capillaries and the lymph in the tissue spaces, a new factor must be considered and that is, the permeability of the capillary wall. This he finds to vary considerably in different parts of the vascular apparatus, being greatest in the capillaries of the liver, less in the capillaries of the intestines and least in the capillaries of the extremities. It also varies doubtless in all other situations. The increase in the production of lymph by the injection of peptones, extract of muscles of the leech, the crab, etc., Starling explains by the assumption that these substances alter the properties of the capillary wall and thus increase its permeability. The difference of pressure, therefore, between blood and lymph taken in connection with the degree of permeability of the capillary wall will account for the production of lymph in all regions of the body.

Another factor that has been invoked to account for the passage of the constituents of lymph across the capillary wall, is an increased concentration of the intercellular lymph, the result of an accumulation of metabolic products, and hence an increase in the osmotic pressure, which would lead to an increase in the passage of the constituents of the blood into the lymph. The activity of a tissue would thus indirectly lead to the formation of lymph.

The Functions of Intercellular Lymph.—The origin and composition of lymph, its situation and relation to the tissue cells indicate that its function is to provide the tissue cells with those nutritive materials necessary to their growth, repair, and functional activities, and to receive from the tissue cells the waste products of their metabolism prior to their removal by the blood- and lymph-vessels.

The necessity for the production of lymph becomes apparent when the chemic changes which the tissues undergo at all times are considered. Thus whether in a state of relative rest or in a state of activity, disintegrative changes are constantly taking place and always in direct proportion to the degree and continuance of the activity. If the tissues are to continue in the performance of their customary activities, it is essential that repair and restoration be at once established. This is made possible by the presence of lymph, and by the power which living material possesses of absorbing from the lymph the necessary nutritive materials, of assimilating them and transforming them into material like unto itself and endowing them with its own physiologic properties.

Coincidently with the loss of nutritive material, the lymph receives the products of the metabolism of the tissues and hence changes in composition. Should this change in composition continue for any length of time, the lymph would lose its restorative character and become destructive to tissue vitality. Therefore it is essential that the nutritive material be renewed as rapidly as consumed and the waste products be carried away as rapidly as produced. Both these conditions are fulfilled by the blood- and lymph-vessels.

The Absorption of Intercellular Lymph.—From the fact that lymph is being discharged from the thoracic duct into the blood, more or less continually, it is evident that lymph is being absorbed from the intercellular spaces; from which fact it may be inferred that the production of lymph is a continuous process and that it is passing through the capillaries in amounts greater than is necessary for the immediate needs of the tissues. Should this excess accumulate there would soon arise the condition of edema and an interference with the functional activities of the tissues. Therefore so soon as the accumulation attains a certain volume it is absorbed in large measure by the lymph-capillaries and transmitted to the lymph-vessels and thoracic duct. Because of the general belief that the lymph-capillaries were in open communication with the tissue spaces it was assumed that the absorption of lymph and its flow through the lymph-vessels was the result of a difference of pressure between the lymph in the tissue spaces and the blood in the innominate veins. But if the lymph-capillaries are closed vessels, as recent investigations indicate, then additional factors, in explanation of lymph absorption, must be sought for.

It is quite possible under even normal conditions of pressure in the tissue spaces that some of the more diffusible constituents of the lymph are absorbed by the capillary blood-vessels. As to whether the relatively feebly diffusible colloids are so resorbed is as yet a matter of investigation.

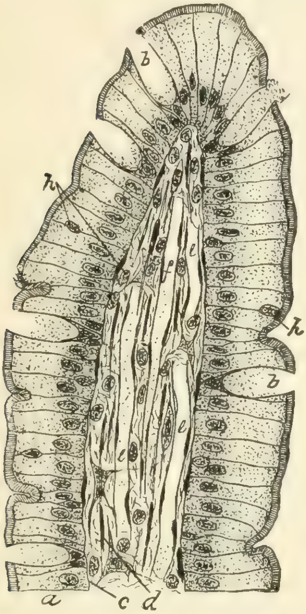

FIG. 88.—LONGITUDINAL SECTION OF A VILLUS FROM INTESTINE OF THE DOG, HIGHLY MAGNIFIED. *a*. Columnar epithelium containing goblet-cells (*b*) and migratory leukocytes (*h*). *c*. Basement membrane. *d*. Plate-like connective-tissue elements of core. *e*, *e*. Blood-vessels. *f*. Absorbent radical or lacteal.—(*Piersol.*)

ABSORPTION OF FOODS

The most important of the absorbing surfaces, especially in its relation to the absorption of new material, is the mucous membrane of the alimentary canal, and more particularly that portion lining the small intestine, provided as it is with specialized absorbing structures—the villi. Though certain substances can be absorbed from the mouth, it is not probable that any food is so absorbed. From the changes which the food principles undergo in the stomach it might naturally be inferred that their absorption would promptly follow. Experimental researches have demonstrated, however, that this takes place, if at all, but to a slight extent. If, however, solutions of inorganic salts, sugars, and peptones possessing a concentration of at least 5 per cent.—a degree of concentration seldom realized under normal conditions—are introduced into the stomach, their absorption will be effected, the rate of absorption following in a general way the increase, within limits, in concentration. Water is practically not absorbed from the stomach. The absorption of the products of digestion—*i.e.*, dextrose, levulose, peptones, amino-acids, soaps, glycerin, fat acids, salts, along with water, in which for the most part they are held in solution—is therefore limited very largely to the small intestine, and is accomplished by the villous processes projecting from the surface of the mucous membrane.

Structure of the Villi.—The villi are small filiform or conical processes, from 0.5 to 1 mm. in length, and from 0.2 to 0.5 mm. in breadth, covering the surface of the mucous membrane from the pyloric orifice to the upper surface of the ileo-cecal valve. Each villus consists of a basement membrane (see Fig. 88) supporting tall columnar epithelial cells. Each cell is composed of granular bioplasm containing a distinct nucleus. At its free extremity a narrow border of the cell presents a striated appearance, as if it were composed of small rods embedded in some cement substance. Goblet or mucin-holding cells are also to be found among the columnar cells. The body of the villus, that portion within the basement membrane, consists of a reticulated connective tissue supporting arteries, capillaries, veins, and lymphoid corpuscles. In the center of the villus there is usually a single, though at times a double, club-shaped lymph-capillary, the walls of which are composed of endothelial cells with sinuous margins. This capillary probably begins by a blind extremity and opens at the base of the villus into the subjacent lymph-vessels. The communicating orifice is guarded by a valve. It is also surrounded by a layer of non-striated muscle-fibers, arranged longitudinally, derived from the muscularis mucosæ and attached to the apex of the body of the villus.

The arteries which penetrate the villi are derived from those of the submucous coat of the intestine, which are the ultimate branches of the intestinal artery, and serve the purpose of delivering nutritive material to the capillary plexus. While passing through the latter a portion of the blood-plasma transudes through the capillary walls into the spaces of the reticulated tissue, constituting lymph. At the same time products of tissue metabolism pass through the capillary walls into the blood. The blood then passes into the venules, which, leaving the villus at its base, unite with the veins of the submucous coat to form the intestinal veins. These finally unite with the gastric and splenic veins to form the portal vein, which enters the liver at the transverse fissure (Fig. 89). The excess of lymph within the villus passes into the club-shaped lymph-capillary, to be finally carried by the lymph-vessels of the mesentery into the thoracic duct. During the intervals of digestion and in the absence of food from the intestine there is, of course, no absorption of food nor the removal from the villus of anything but the excess of lymph and metabolic products.

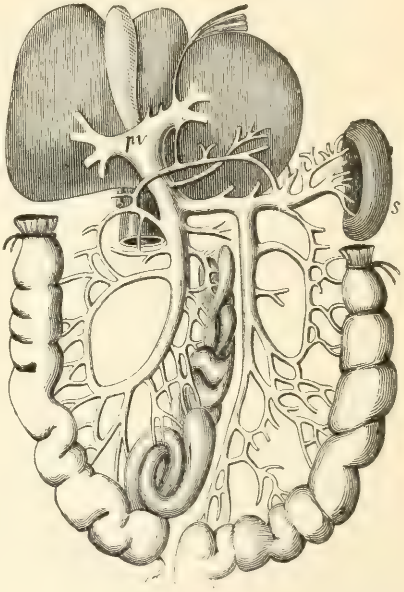

Fig. 89.—Diagram of the Portal Vein (*pv*) arising in the Alimentary Tract and Spleen (*s*), and Carrying the Blood from These Organs to the Liver. —(*Yeo's "Text-book of Physiology."*)

Function of the Villi.—The villi, and especially the epithelial cells covering them, are the essential agents in the absorption of the products of digestion. It is by the activity of these cells that the new materials are taken out of the alimentary canal and transferred into the lymph-spaces in the interior of the villi, from which they are subsequently removed by the blood-vessels and lymph-vessels. As to the mechanism by which the epithelial cells accomplish this result, nothing definite can be asserted. Inasmuch as the absorption of food does not take place in accordance with the laws of osmosis as at present understood, it has been suggested that the cells possess a "selective action" dependent on their organization and physiologic activity, an activity which is to a great extent conditioned and limited by the degree of diffusibility of the substances to be absorbed.

Absorption of Water and Inorganic Salts.—Water and inorganic salts after their absorption from the intestine and transference into the lymph-spaces of the villi pass through the walls of the capillary blood-vessels and are carried, by the blood of the portal vein, into and through the liver into the blood of the general circulation. Unless water be present in excessive amounts, there is no appreciable absorption of water by the lymph-vessels.

Absorption of Sugar.—As previously stated, all the carbohydrates, with the exception possibly of lactose, are transformed by the digestive fluids into either *dextrose* or *levulose*, under which forms they are absorbed by the epithelial cells. It is possible, however that soluble dextrin may also be absorbed. Whatever the form under which the carbohydrates are absorbed, they never leave the epithelial cells except as dextrose and levulose. Direct experimentation has shown that the sugars are taken up by the capillary blood-vessels and carried direct to the liver. Analysis of the blood of the portal vein after the ingestion of large quantities of sugar may reveal an increase to 0.25 per cent.; while after the injection of sugar into the intestine the percentage may rise as high as 0.4 per cent. As chemic analysis of lymph obtained from the thoracic duct shows no increase in the percentage of sugar beyond that normally present (0.1 per cent.), it is assumed that sugar is not removed from the villi by the lymph-vessels.

On reaching the liver a portion of the sugar 12 to 20 per cent. passes from the blood stream across the walls of the capillaries into surrounding lymph spaces and comes into direct relation with the liver cells. Then through the agency of an enzyme, the sugar is dehydrated, converted into starch and stored for a variable length of time in the liver cells in the form of hyaline masses which can be readily seen with the aid of the microscope. Under this form the carbohydrate material is retained until the necessity arises for its return to the blood, and this happens, when the percentage of sugar in the blood falls below the normal, viz.: 0.10 to 0.15 per cent. Under such circumstances the necessary amount of the liver starch is hydrated, converted into sugar, and passed into the blood in quantities sufficient to restore the normal percentage. The apparent necessity for this temporary storage of sugar in the liver is to prevent its too rapid entrance into the arterial blood and hence a rise in the percentage far beyond that which is normal. Should this occur a condition known as hyperglycemia would result and as a consequence an elimination of the excess by the kidneys giving rise to the condition known as glycosuria.

Absorption of the Products of Protein Digestion.—For the reason that the proteins are for the most part transformed through hydration and cleavage by the action of the gastric and pancreatic enzymes into peptones and for the further reason that the peptones are diffusible bodies, it was formerly believed that they represented the final stages in the digestion of the proteins, and as such were absorbed out of the intestinal contents by the action of the epithelium covering the villi. Inasmuch as chemic analysis failed to detect more than a trace of either peptone or native protein in the portal blood or in the lymph of the thoracic duct, it was assumed that the epithelium after absorbing, also synthesized them into some form of coagulable protein (plasma-albumin) which is readily assimilable by the blood. The plasma-albumin thus supposed to be formed by the epithelial cells was believed to pass into the interior of the villus, thence into the blood by which it was carried to the liver. After passing through this organ it entered the blood of the general circulation and became a part of the common store of protein, out of which each tissue cell constructed the particular protein characteristic of it. That such a conversion of peptones to plasma-albumin would be necessary in case of their absorption would appear from the fact that the introduction of peptones even in small amounts into the blood is followed by their elimination unchanged in the urine. When injected into the blood in large amounts, they act as toxic agents, giving rise to a fall of blood-pressure, a diminished coagulability of the blood, coma, and death.

This general view as to the absorption of peptones is no longer entertained. There are reasons, however, for believing that the change which proteins undergo in digestion, is more far-reaching and complete, and that the peptones in turn are disintegrated and reduced to even simpler bodies such as polypeptids, peptids and amino-acids (see page 191). The extent to which this disintegration proceeds will doubtless depend, to some extent, on the quantity and variety of proteins consumed.

Since recent investigations make it highly probable that the final stage in the digestion of protein is the formation of amino-acids it has come to be believed that the problem of absorption is to be transferred to these fragmentary bodies rather than to the peptones. Assuming this to be true, the question at once arises as to what change, if any, they undergo during their passage through the intestinal epithelium. The difficulty of detecting the presence of amino-acids in the blood led to the assumption that after their absorption they were synthesized, just as the peptone molecules were supposed to be, and a protein molecule constructed similar to, if not identical, with plasma-albumin.

The recent investigation of Abel, carried out with a new form of diffusion apparatus, renders it highly probable that amino-acids are present in the circulating blood in readily determinable quantities. This has led to the belief that the amino-acids, in part, at least, are absorbed as such, pass through the intestinal epithelium, the portal blood and the liver unchanged, and enter the blood of the general circulation to be carried by it directly to the tissues where they are at once utilized by the tissue cells or stored for future use. This view renders it much easier to understand, how out of the different proteins of the foods, varying widely in their composition, the specific proteins of the tissues are constructed. It is only necessary to assume that the tissue cells select from the variety of amino-acids presented to them, only those which are necessary to the formation of the protein by which they are characterized. The plasma-albumin, whatever its origin, might then be regarded as a protein surplus to be called on if the protein ingested should be insufficient. It may be, however, that future investigations will ascribe other functions to it.

Under whatever form the protein material is absorbed there is every reason to believe that it is carried by the portal circulation to the liver, through which it passes to enter the blood of the general circulation. Ligation of the thoracic duct does not interfere to any appreciable extent with protein absorption nor with the normal production and elimination of urea, nor with the weight of the animal.

Many facts in the physiologic chemistry of the body raise the question as to what percentage of the amino-acids produced in the intestine daily is utilized for tissue repair and growth. If the protein requirements of Chittenden, viz.: 58 to 60 grams only, are necessary for repair and growth, then approximately one-half the amino-acids produced from the protein usually consumed must be disposed of in some other manner. The manner of disposal of these unused (that is, unused for tissue repair and growth) fragments of protein disintegration is doubtless varied; some of the amino-acids, after absorption by the epithelial cells of the villi and mucosa, are deprived of NH_2 (the amino-acid nitrogen) or deaminized; the NH_2 is then converted into ammonia, combined with carbon dioxid to form ammonium carbonate, carried to the liver, and changed into urea. That this is very probably the case is rendered likely from the presence of a large quantity of ammonia in the mucous membrane of the intestine and in the blood of the portal vein, in which after a meal rich in protein it may be four times as great as in the arterial blood. The remainder of the amino-acid molecule is changed into some carbonaceous radical and finally into sugar or fat and subsequently utilized by the organism for heat production. The dynamic portion of the amino-acid is this deaminized remainder. Other of the surplus amino-acids are acted on by intestinal bacteria, and converted into simpler compounds, after which they are eliminated in the feces or absorbed and carried to the liver where they undergo other changes and eventually appear in the urine.

The ammonia set free during digestion is absorbed, carried to the liver and transformed to urea.

Absorption of Fat.—As previously stated, there are two views as to the changes which fats undergo during digestion. According as the one or the other is accepted will depend the view as to the nature of the absorptive process. If it be assumed that the final stage in the digestion of fat is a purely physical one, the production of an emulsion in which the fats present themselves as fine granules, it is difficult to give any satisfactory explanation of the mechanism by which the epithelial cells take them up. Various theories have been advanced to explain the process, but none are free from serious objections. This view of fat absorption has largely been based on the observation that during digestion fatty granules can be seen in all portions of the cell apparently passing toward the interior of the villus.

If, on the contrary, it be admitted that the final stage in the digestion of fats is the formation of soaps and glycerin, both of which are soluble, their absorption can more readily be accounted for. According to this view, the soaps and glycerin are again synthesized by a process the reverse of that which is brought about by the pancreatic enzyme, with the appearance of minute granules of fat. That this is the more probable view as to the mechanism of fat absorption is evident from the fact that when animals are fed with alkaline soaps and glycerin, or with fatty acids alone, globules of fat are found in the epithelial cells and in the interior of the villus.

With the passage of the fat-granules into the interior of the villus they at once enter the lymph-radicle and become constituents of the lymph-stream, to which they impart a white, milky appearance. If the abdomen of an animal in full digestion be opened, the lymph-vessels of the mesentery present themselves as distinct white threads. An examination of the fluid they contain, known as *chyle*, shows the presence of fat-granules of microscopic size. With the passage of the chyle into the thoracic duct it also assumes the same milky appearance. For this reason the lymphatics of the mesentery were erroneously termed *lacteals*. The chyle as obtained from these lymph-vessels possesses the same qualitative though not quantitative composition as lymph, the difference being mainly in the large excess of fat in the former. Indeed, chyle may be regarded as lymph with the addition of fat.

With the absorption of the last of the fat-granules the contents of the lymph-vessels of the mesentery—the lacteals—begin to lose their white appearance near the intestine and as the fat-granules pass toward the thoracic duct, the lymph-vessels gradually become transparent and disappear from view. A similar change in the appearance of the thoracic duct ensues, as the last portions of the fat ascend the duct to be discharged into the blood-stream.

Routes for the Absorbed Food.—Physiologic experiments have demonstrated that the agents concerned in the removal of the products of digestion after their absorption from the interior of the villus are:

1. The veins of the gastro-intestinal tract, which converge to form the portal vein.
2. The lymph-vessels of the small intestine, which converge to empty into the thoracic duct.

The products of digestion find their way into the general circulation by these two routes, as follows: (See Fig. 90.)

The water, inorganic salts, proteins or amino-acids, and sugar after entering the blood-vessels of the villus are carried by the blood of the intestinal veins directly into the liver by the portal vein; after circulating through the capillaries of the liver and being influenced by the liver cells, they are discharged by the hepatic veins into the inferior or ascending vena cava.

The fat-granules, synthesized in the epithelial cells, after entering the lymph-radicle of the villus are carried by the lymph-stream of the intestinal lymph-vessels and emptied into the receptaculum chyli from which they ascend into the thoracic duct, by which they are discharged into the blood at the junction of the left subclavian and internal jugular veins.

Forces Aiding the Movement of Lymph and Chyle.—The force which primarily determines the movement of the lymph has its origin in the beginnings of the lymph-vessels, the lymph-spaces, and depends on a difference in pressure here and at the termination of the thoracic duct. The rise of pressure in the lymph-spaces is due to the continual production of lymph, either by filtration or secretor activity of the capillary walls. As soon as the pressure rises above that in the thoracic duct a forward movement of lymph takes place. Other things being equal, the rate of movement will be proportional to the difference of pressure. The first movement of the chyle, its passage from the lymph-capillary in the villus into the subjacent lymph-vessel, has been attributed to a shortening of the villus and a

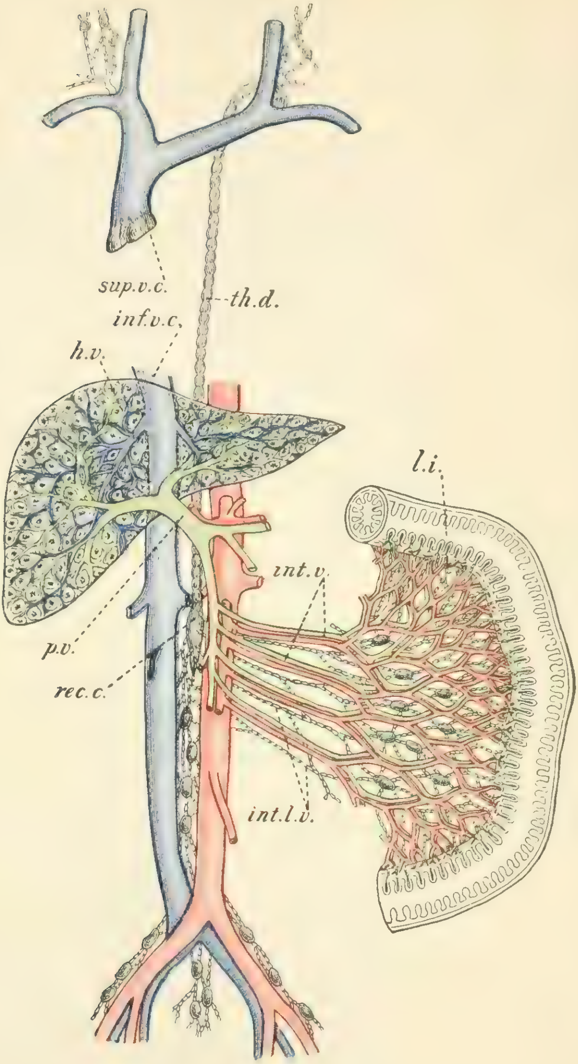

FIG. 90.—DIAGRAM SHOWING THE ROUTES BY WHICH THE ABSORBED FOODS REACH THE BLOOD OF THE GENERAL CIRCULATION (*G. Bachman*). *l. i.*, Loop of small intestine; *int., v.*, intestinal veins converging to form in part, *p. u.*, the portal vein, which enters the liver and by repeated branchings assists in the formation of the hepatic capillary plexus; *h. u.* the hepatic veins carrying blood from the liver and discharging it into, *inf. v. c.*, the inferior vena cava; *int. l. v.*, the intestinal lymph vessels converging to discharge their contents, chyle, into *rec. c.* the receptaculum chyli, the lower expanded part of the thoracic duct; *th. d.*, the thoracic duct discharging lymph and chyle into the blood at the junction of the internal jugular and subclavian veins; *sup. v. c.*, the superior vena cava.

compression of the capillary by the contraction of the non-striated muscle-fibers by which it is surrounded. With the entrance of the chyle into the subjacent lymph-vessel there is a distention of the vessel and a rise in pressure. When the muscle-fibers relax, regurgitation is prevented by the closure of the valves at the base of the villus. The elastic tissue of the lymph-vessel now recoils and forces the chyle toward the thoracic duct. After the emptying of the lymph-capillary the conditions as far as pressure is concerned are favorable for the absorption of new material. The rhythmic contractions of the intestinal wall undoubtedly aid in the movement of lymph and chyle. It is quite possible that the walls of the general lymphatic system aid the forward movement of lymph by more or less rhythmic contractions of their contained muscle-fibers.

Inasmuch as the lymph-vessels lie in situations in which they are subject to compression by muscles during contraction, it is probable that the fluid in the vessels will be forced onward toward the thoracic duct at each compression, a backward movement being prevented by the closure of the valves which are everywhere present in the vessels. Experimental observations have demonstrated the truth of this supposition. Alternate contraction and relaxation of the muscles of the leg will, in an animal at least, increase considerably the flow as well as the production of lymph from the thoracic duct. Massage has a similar influence.

The respiratory movements also aid the flow of both lymph and chyle from the thoracic duct and larger lymph-vessels into the venous blood. During inspiration the intrathoracic pressure (that is, the positive pressure exerted by the air in the lungs on the intrathoracic viscera, *e.g.*, heart, veins, thoracic duct, etc., which is less by about 6 millimeters of mercury than the pressure in the lungs) decreases. The decrease is proportional to the extent of the inspiration. With this decrease of pressure, the thoracic duct expands and its internal pressure falls. As the intra-abdominal portion of the thoracic duct and its tributaries are subjected to a higher pressure, practically that of the atmosphere the lymph in these vessels is forced, by reason of the difference in pressure between these two regions, into the intrathoracic portion of the duct. During expiration, the rise of the intrathoracic pressure to its former value leads to a compression of the thoracic duct and causes the lymph to be discharged rapidly into the blood-stream. A regurgitation of the lymph is prevented by the closure of the numerous valves throughout the course of the duct.

DIFFUSION. OSMOSIS. FILTRATION

As these three factors are believed to play an important part in many physiologic processes, it is essential to a better understanding of these processes, that certain elementary facts relating to these three factors be known.

Diffusion.—By diffusion is meant the gradual and spontaneous mixture of the molecules of two or more liquids, or of two or more gases, when brought into contact with each other, without the application of an external force. The reason for both processes lies in the fact that the molecules of a liquid and of a gas are in constant motion, in consequence of which a mutual interpenetration of the molecules takes place, which continues until a condition of homogeneity is established.

Again, when a soluble substance, inorganic or organic, is placed in water, the molecules of the substance will at once begin to separate themselves and to diffuse throughout the water until the solution becomes homogeneous, and notwithstanding the fact that the dissolved substance possesses weight, the solution remains homogeneous. The force of gravity is overcome by the force of diffusion.

The velocity with which the molecules of a substance will diffuse through a solvent like water, varies considerably. The experiments of Graham show that if the molecules of a given weight of hydrochloric acid diffuse completely in a unit of time, the molecules in the same weight of sodium chlorid, cane-sugar, albumin and caramel, will require for their diffusion 2.33, 7, 48, and 98 units of time respectively.

Osmosis.—Osmosis may be defined as the passage of the molecules of water through an intervening membrane. If the water on one side of the membrane, parchment for example, contains in solution substances such inorganic salts, their molecules will also pass through the membrane though the time required for this to take place may be much longer than in the case of the water molecules. The passage of the dissolved substance through the membrane though usually included under the term osmosis is more properly termed dialysis.

If the two volumes of water on opposite sides of the membrane are the same in amount, and if the one volume contains a salt in solution, the salt molecules will continue to pass through the membrane until the water on both sides contains the same number of molecules, or, in other words, until it is homogeneous in composition. The time required for their passage being longer than the time required for the passage of the water molecules, there will be (owing to factors which will be explained later), a temporary increase in the volume of the water originally containing the salt, but in time the two volumes will again become equal. Certain other substances which may be in solution, such as albumin, starch, etc., will not pass across a membrane, because of the large size of their molecules. Graham termed all those substances which by virtue of the small size of their molecules pass through membranes, *crystalloids*, and all those which by virtue of the large size of their molecules do not pass through membranes or to a very slight extent, *colloids*.

It was stated in the foregoing paragraph that if two equal volumes of water are separated by a parchment septum, one of which contains in solution an inorganic salt, the molecules of the salt-free water will osmose through the septum into salt-containing water, more rapidly than they will in the opposite direction, and as a result, there will be a temporary increase in the volume of the water containing the salt. If the membrane were impermeable to the salt molecules, the difference in the two volumes of the water would be far more permanent and striking. The reason assigned for this is that the molecules of the salt exert a pressure against the outer layer of the water molecules and these in turn against the membrane, in consequence of which there is a more rapid osmosis of the water molecules towards the salt than in the reverse direction. To this pressure is applied the term

Osmotic Pressure.—Osmotic pressure may be defined as the pressure exerted by the molecules of the substance in solution against the outer layer of the molecules of the solvent. If the solvent is enclosed by an elastic membrane it is expanded and in consequence there is an osmosis of a surrounding solvent towards and through it. The reason for this pressure lies in the fact that, when the molecules of a substance are separated a certain distance, as they are when in solution, they repel one another as do the molecules of a gas and in their flight strike against the outer layer of the solvent. The pressure of the molecules of a substance in solution is therefore comparable to the pressure of the molecules of a gas.

Three methods may be employed for measuring the force of the osmotic pressure of different substances, viz.: 1. Physical. 2. The determination of the freezing point. 3. By calculation.

1. *Physical Method.*—For the purpose of measuring osmotic pressure by physical methods, it is customary to make use of an apparatus similar to that represented in Fig. 91, which consists of an earthenware vessel (*a*), into the upper open end of which a tall vertical glass tube has been hermetically sealed. The pores of the earthenware vessel have been filled by a membrane made by precipitating ferrocyanid of copper within them. This membrane is freely permeable to water, but impermeable to certain substances in solution, *e.g.*, cane-sugar. Such a membrane, which permits the passage of the molecules of the solvent but not the molecules of the dissolved substance, is termed a semi-permeable membrane, and its use is absolutely necessitated when it is desired to obtain the actual pressure exerted by any given substance in solution. An apparatus of this character is termed an osmometer.

When, therefore, the osmometer containing a solution of cane-sugar is placed in the vessel (*b*) containing water, the following phenomena occur, viz.: an ascent of the cane-sugar solution in the vertical glass tube, and a descent of the level of the water in the vessel *b*. These phenomena continue until the level of the fluid in the glass tube reaches a certain height, when it becomes stationary, and no further effect takes place.

In explanation of the foregoing phenomena it may be said that the molecules of the sugar strike or press against the outer layer of the molecules of the solvent, which at all points are in contact with the rigid walls of the earthenware vessel, except at the open extremity of the vertical glass tube. Inasmuch as the rigid walls of the osmometer prevent any outward displacement of the molecules of the water, the force of the impact of the sugar molecule is directed against the molecules at the extremity of the vertical tube which are in consequence pressed or pushed upward a certain distance. Because of the loss of energy due to the impact, the sugar molecule does not rebound with the same velocity, and hence time is permitted for the molecules of the water to pass into the sugar solution, to occupy the space, and thus maintain the level of the fluid in the vertical tube. (For the reason that the osmometer is permeable to water, the molecules will pass outward as well as inward though more will pass in a unit of time in the latter, than in the former direction, until equilibrium is established.) The pressure of the sugar molecules continuing, the level of the fluid in the glass tube continues to rise and the level of the fluid in the vessel, *b*, continues to fall until the force of gravity prevents any further upward movement of the molecules of sugar against the outer film of the molecules of the water. The difference in the level of the two fluids expressed in millimeters of mercury is taken as a measure of, and equal to, the pressure of the sugar in solution. A 1 per cent. solution of cane-sugar at a temperature of from 13°C. to 16°C., as determined by this method, exerts an osmotic pressure of about 535 mm. Hg.; a 2 per cent. solution exerts an osmotic pressure approximately twice this amount.

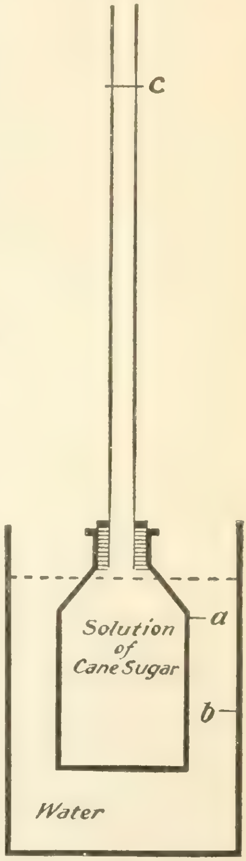

Fig. 91.—An Osmometer.

Experiments made with this and similar osmometers show—

1. That the osmotic pressure of any substance in solution is proportional to the concentration, providing the temperature is constant.
2. That when the concentration is constant the osmotic pressure rises with, and is proportional to, the temperature.

3. That when different substances are present in the same solvent the osmotic pressure is equal to the sum of the individual or partial pressures.
4. That whatever the nature of the substance in solution it will exert the same osmotic pressure, providing always the same number of molecules are present; hence the molecular weights in grams per liter of different substances exert the same osmotic pressure at the same temperature.

Because of the fact that when certain substances, *e.g.*, many inorganic salts, many acids and bases, are dissolved, some of their molecules undergo ionization, *i.e.*, separation into parts which are charged with electricity, and hence the two together, molecules and ions, exert a greater osmotic pressure than would otherwise be the case; and because of the further fact, that it is extremely difficult to obtain absolutely semipermeable membranes, uniform results are not obtained by the employment of the three methods; therefore, the osmometric methods as well as the calculation or arithmetic method have been largely discarded and the method based on the determination of the freezing point has been adopted.

2 *The Determination of the Freezing Point.*—Because of the difficulty in obtaining the exact osmotic pressure by means of the osmometer as stated above, reliance is now placed on the mathematic relation known to exist between osmotic pressure and the freezing point. Thus the freezing point of water holding any substance in solution is lower than water itself and is indeed proportional to the number of molecules dissolved. As a standard of comparison it is customary to employ a gram-molecule of a substance dissolved in one liter of water. (A gram-molecule is the quantity of a substance expressed in grams equal to its molecular weight.) The lowering of the freezing point of a gram-molecule solution below that of water is constant, viz., 1.87°C. The osmotic pressure therefore of such a solution, as determined by calculation (see below), is equal to 22.38 atmospheres, or 17,008 mm. of Hg.

Therefore it is only necessary to determine by means of a differential thermometer the lowering of the freezing point in degrees centigrade, which is usually expressed by the symbol $\triangle$. Then the osmotic pressure is equal to $\triangle$ divided by 1.87° C., and multiplied by 22.38 atmospheres, or 17,008 mm. of Hg. Thus if the freezing point of any solution was found to be 0.83°C. lower than water, its osmotic pressure would be $0.83 \div 1.87 \times 22.38$ atmospheres or 9.847 atmospheres $= 7{,}483$ mm. Hg. If any two solutions have the same freezing point they contain the same number of molecules and hence have the same osmotic pressure. Blood plasma has a freezing point of 0.56°C. Experimentally it has been determined that the freezing point of water is lowered to the same level, when it contains sodium chlorid to the extent of 0.95 per cent. Hence these two fluids have the same osmotic pressure and are *isotonic;* each exerts a pressure of 6.696 atmospheres.

For this reason the sodium chlorid solution can be employed for preserving, for a time at least, the form of blood corpuscles or other living mammalian cells, from which it may be inferred, that the contents of the cells have an osmotic pressure approximately equal to that of the blood plasma or the salt solution. If the salt solution has a lower concentration and hence a lower osmotic pressure, water will osmose into the corpuscle and cause a discharge of its hemoglobin content. Such a fluid is said to be *hypo-isotonic.* If, on the contrary, the salt solution has a higher concentration and hence a higher osmotic pressure, water will osmose from the corpuscle causing a shrinkage and crenation of the corpuscle. Such a fluid is said to be *hyperisotonic.*

3. *By Calculation.*—The osmotic pressure may also be obtained by calculation based on the known pressure exerted by a gram-molecule of hydrogen—2 grams—when compressed to a volume of one liter. It is well known that 1 gram of hydrogen at 0°C. and at an atmospheric pressure of 760 mm. Hg. occupies a volume of 11.19 liters, and that 2 grams under the same conditions will occupy a volume of 22.38 liters, and that when the two grams, that is, one gram-molecule is com-

pressed to a volume of 1 liter the molecules will exert a pressure equal to that of 22.38 liters or 22.38 atmospheres or 17,008 mm. of Hg. Since a gram-molecule of any substance dissolved in 1 liter of water contains the same number of molecules as a gram-molecule of hydrogen compressed to one liter, they have the same osmotic pressure.

From this it is possible to calculate the osmotic pressure of an electrolyte, if the percentage composition of the substance in solution be known. Let it be supposed, for example, that it is desirable to know the osmotic pressure of a 1 per cent. solution of cane-sugar. The procedure is as follows: A gram-molecule of cane-sugar ($C_{12}H_{22}O_{11}$) contains 342 grams; a 1 per cent. solution contains 10 grams to the liter; hence its osmotic pressure is $10 \div 342 \times 22.38$ atmospheres or 0.65 atmosphere which is equal to 494 mm. of Hg.

Filtration.—Filtration may be defined as the passage of water, and of all substances dissolved in it, through a membrane as a result of a difference of hydrostatic pressure on the two sides. The difference between the two pressures constitutes the force of filtration, and hence the greater the difference, the greater will be the amount of fluid filtered.

With any given artificially prepared animal membrane the quantities of water and crystalloids in general which pass through the membrane are proportional to the filtration force, and hence the filtrate will have a concentration similar to, if not identical with, that of the original solution. The passage of colloids in solution will be proportional to the permeability of the membrane and an increase in the filtration force. The filtrate, however, will have a lower degree of concentration than the original solution for the reason that as the pressure rises the quantity of water filtered increases in a greater ratio than the quantity of colloid filtered.

Physiologic Applications.—In the animal body the fluids are separated by delicate membranes through which the constituents of the fluids, inorganic and organic, are continually passing. Thus prepared foods in the intestine pass through the intestinal wall into blood- and lymph-vessels; the constituents of the blood pass through the wall of the capillary vessel into the tissue spaces from which they pass (*a*) through the walls of various glands to take part in the formation of their secretion; (*b*) through the sarcolemma into the interior of the muscle fiber; (*c*) through the limiting surface of, and into the interior of all other tissue cells. The waste products, the result of tissue and food metabolism, pass from the interior of cells through their limiting membranes or surfaces into the tissue spaces; thence through the wall of the capillary vessel into the blood and finally through the wall of the capillary vessel and the epithelium of the lung, the kidney, the liver, etc., to take part in the formation of the excretions. These and other processes are believed to be accomplished by the factors, diffusion, osmosis, and filtration.

The statements that have been made in foregoing paragraphs in reference to diffusion, osmosis, and filtration have been based on the results of experiments which have been made with non-living membranes, and under conditions purely physical; and though it is quite true that in the animal body the fluids are separated by membranes more or less permeable to all their constituents, and that all pass through these membranes, it is possible that the facts which have been obtained experimentally are not strictly paralleled in the living body, and hence not strictly applicable to the elucidation of physiologic processes. Nevertheless there are reasons for thinking that a thorough understanding of these factors will eventually throw much light on the intimate nature of the process by which organic as well as inorganic substances in solution pass through animal membranes in the living condition.

CHAPTER XII

THE BLOOD

The blood may be defined as the nutritive fluid of the body since it contains all those materials that are necessary to the maintenance of the nutrition. The presence and proper circulation of the blood in the living organism are essential for the maintenance of tissue irritability and for the manifestation of the activities of all physiologic mechanisms. The escape of the blood from the vessels, especially in the higher animals, is followed by cessation of the physiologic activities of all the tissues within a short period. The irritability, however, persists for a variable length of time though it too gradually declines and finally disappears. The immediate dependence of the functional activities of the tissues and organs on the presence of the blood can be demonstrated by the following experiment: If the nozzle of a syringe, adapted to the size of the animal, be introduced through the jugular vein into the right side of the heart and the blood be suddenly withdrawn, there is an immediate cessation in the activity of all the organs; the return of the blood to the vessels within a limited period of time is promptly followed by a renewal of their activity.

Though contained within a practically closed system of vessels, the blood is brought into intimate relation with all the tissue elements through the intermediation of the capillaries. As the blood flows through these delicate vessels, portions of its soluble nutritive constituents, including oxygen, are given up to the tissues, by which they are utilized for growth, repair, and the liberation of heat. At the same time the tissues yield up to the blood a series of decomposition or katabolic products, resulting from their activity, which vary in quantity and quality according as the blood traverses the muscles, nerves, glands, or other tissues.

The blood may be regarded, therefore, as a reservoir of nutritive materials prepared by the digestive apparatus and absorbed from the intestinal canal; of oxygen, absorbed from the respiratory surface of the lungs; of katabolic products, produced by and absorbed from the tissues. Though the blood varies in composition in different parts of the body in consequence of the introduction of both nutritive material and katabolic products, it nevertheless presents certain average physical, morphologic, and chemic properties which distinguish it as an individual tissue.

The Physical Constitution of Blood.—A microscopic examination of the blood as it flows through the capillary vessels of the web of the frog or the mesentery of the rabbit shows that it is not a homogeneous fluid, but that it consists of two distinct portions, viz.: (1) a clear, transparent, slightly yellow fluid, the *plasma* or *liquor sanguinis:* (2) small particles termed corpuscles floating in it, of which there are two varieties, the *red* or the *erythrocytes* and the *white* or the *leukocytes.* By appropriate methods it can be shown that a third corpuscle, colorless in appearance and smaller in size than the ordinary white corpuscle, is present in the blood-stream and known as the *blood-platelet* or *plaque.* The different constituents can be roughly separated by appropriate means when the blood is withdrawn from the body. If the blood of the horse is allowed to flow directly into a tall cylindric glass vessel, surrounded by ice, it separates in the course of a few hours into three distinct layers in accordance with their specific gravities. The lower layer is dark red and consists of the red corpuscles; the middle layer is grayish in color and consists of the white corpuscles; the upper layer is clear and transparent and consists of the plasma. The red corpuscles occupy almost one-half, the white one-fortieth, the plasma a trifle more than one-half of the height of the entire blood-column, which indicates approximately the different volumes of each. The same result can be obtained with human blood by the use of the centrifuge or hematocrit.

PHYSICAL PROPERTIES OF BLOOD

1. **Color.**—Within the blood-vessels two kinds of blood are distinguished—the *arterial,* the color of which is a bright scarlet-red, and the *venous,* the color of which is a dark bluish-red or purple. The cause of the color as well as the difference in color is the presence in the red corpuscles of coloring-matter, hemoglobin, in different degrees of combination with oxygen. The intensity of the color in either kind of blood is dependent on the thickness of the blood-stream, for in the finest capillaries, as seen under the microscope, there is an almost total absence of color. As the venous blood passes into and through the pulmonic capillaries the hemoglobin absorbs a certain volume of oxygen after which it changes in color and on emerging from the lungs imparts to the blood its characteristic scarlet-red color. By reason of the union of the hemoglobin with the oxygen it is generally termed while in the arteries, oxyhemoglobin. As the arterial blood passes into and through the systemic capillaries, the oxyhemoglobin yields up a portion of its oxygen to the tissues after which it again changes in color and on emerging from the tissues imparts to the blood its characteristic bluish-red color. By reason of the loss of a portion of its oxygen, the hemoglobin is generally termed while in the veins, deoxy- or reduced hemoglobin.

2. **Opacity.**—Owing to the fact that the corpuscles have a refracting power different from the plasma, the blood, even in thin layers, is opaque. The repeated refractions and reflections which light undergoes in passing through plasma and corpuscles is attended by such a dissipation that it is impossible to see printed matter through it. That the opacity is due to the shape of the corpuscles rather than to their contained coloring-matter is evident from the fact that when the hemoglobin is caused to separate from the corpuscles by the addition of chemic reagents, the blood, though it deepens in color, at once becomes transparent.

3. **Odor.**—When freshly drawn the blood possesses a peculiar characteristic odor which has been attributed to the presence of a volatile fat acid in combination with an alkaline base. The intensity of the odor may be increased by the addition of concentrated sulphuric acid, by means of which the volatile acid is set free.

4. **Specific Gravity.**—The specific gravity of blood lies within the limits of 1.051 and 1.059, averaging in man 1.056 and in woman 1.053. Normally,

variations from these values are only temporary and are connected with variations in physiologic processes. The specific gravity is diminished by the ingestion of liquids and abstinence from solid food. It is increased by abstinence from liquids, by the ingestion of dry food, and by the elimination of large quantities of water by the lungs, skin, and kidneys.

Inasmuch as the specific gravity of the blood varies from the normal in one direction or the other in certain pathologic states, it is deemed desirable for clinical purposes to determine the extent of this variation. Among the methods suggested for this purpose that of Hammerschlag is the one most generally resorted to. It is based on the principle, that a fluid in which a drop of blood neither rises nor falls must have the same specific gravity as the blood itself. As the specific gravity of the blood varies in different pathologic states it is essential that the fluid employed is of such a character that its specific gravity can be quickly varied in one direction or the other. To meet this indication a fluid, a mixture of chloroform (specific gravity 1.526) and benzol (specific gravity 0.889) is first prepared in such proportions that the mixture has a specific gravity of about 1.040. With a pipette a drop of blood is then placed in the mixture. If the drop rises the specific gravity of the mixture is greater than that of the blood. Benzol is then gradually added until the drop remains stationary. At this moment the specific gravity of the mixture is the same as that of the blood. If the drop falls the specific gravity of the mixture is less than that of the blood. Chloroform is then gradually added until the drop remains stationary. At this moment the specific gravity of the mixture is the same as that of the blood. In either case the specific gravity of the mixture is determined with a suitable hydrometer and the figure observed attributed to the blood.

5. **Reaction.**—The reaction of the blood has usually been stated as alkaline from its effect on litmus paper. Thus, if blood is permitted to remain for a few seconds on slightly reddened glazed litmus paper and then washed off, a distinct blue color presents itself against a red or violet background. The alkalinity thus indicated has been attributed to disodium phosphate, Na_2HPO_4, and sodium carbonate, Na_2CO_3. The degree of the alkalinity is measured by the amount of a standard acid necessary to be added before the indicator used shows an acid reaction. According to v. Jaksch the alkalinity corresponds to from 260 to 300 milligrams of sodium hydrate, NaOH, for every 100 c.c. of blood, according to Löwy from 300 to 325 milligrams. The hitherto unavoidable error in these estimates is about 30 milligrams. The alkalinity from this point of view varies but within narrow limits in physiologic conditions. It is increased in the early stages of digestion and decreased in the later stages as well as after prolonged exercise.

In accordance with the ideas of physical chemistry the acidity of a fluid is dependent on the presence of hydrogen ions, H^+, and the alkalinity on the presence of hydroxyl ions, $(\overline{OH})$. The reaction of any fluid, containing a number of chemic compounds in solution, will be dependent therefore on the relative proportions of hydrogen ions and hydroxyl ions that make their appearance.

If the hydrogen ions are in excess the fluid is acid, if the hydroxyl ions are in excess the fluid is alkaline in reaction. Tested by the methods of physical chemistry blood and lymph are found to possess these opposite ions in equal degree and therefore are neither acid nor alkaline but neutral in reaction.

6. **Temperature.**—The temperature varies in degree in different parts of the body. If the temperature variations correspond with the variations in some other mammals, the highest temperature is in the hepatic veins where, as in the dog, it registers about 40.6°C., and the lowest temperature is near the surface as in the mouth and axilla, where it is approximately 38.9°C.

7. **Viscosity.**—Viscosity may be defined as the resistance to the movement of the molecules of a fluid homogeneous body among themselves. In accordance with the degree of this resistance, which may also be spoken of as internal friction, will the fluid at a given temperature be mobile or viscous. Viscosity varies partly with the nature of the fluid and partly on its temperature. Thus at the same temperature water, syrup, and pitch possess different degrees of viscosity. A rise in temperature of 1°C. diminishes the viscosity about 2 per cent. In all discussions relating to the viscosity of fluids, that of distilled water is taken as a standard and regarded as unity.

Blood as a fluid is regarded by physiologists as possessing viscosity, though the definition in the foregoing paragraph is not strictly applicable, as it is not a homogeneous but a heterogeneous fluid consisting of plasma the molecules of which show an inner friction and of corpuscles which also show friction. Blood having a complex composition as compared with water has naturally a greater degree of viscosity or internal friction. Experimental investigations render it certain that the observed viscosity is dependent on the corpuscular elements to a greater extent than on the composition of the plasma. About two-thirds of the viscosity is due to the corpuscles.

The viscosity of blood as compared with water may be determined by permitting the two fluids to flow through capillary tubes of corresponding caliber under a steadily acting pressure and then determining the volume that flows through each in a given time, or by determining the distance to which each fluid flows in a unit of time in these capillary tubes and then in each instance, comparing the results one with the other. Normal human blood is thus found to possess a viscosity 4.5 times that of distilled water at body temperature. Dog's blood has a viscosity 6 times that of water. If the temperature of blood is raised the viscosity diminishes. Recalling the statement that the viscosity is closely connected with the presence of red corpuscles it would be expected that either an increase or decrease in their number would change the viscosity in one direction or another. In a case of polycythemia in which the red corpuscle count was 11,000,000 per cubic millimeter the viscosity was between 3 and 4 times the normal. In certain other pathologic states of the blood characterized by a diminution in the number of red corpuscles the viscosity diminished one-half or more. The ingestion of meat raises the viscosity, while the ingestion of fats and carbohydrates diminishes it.

The determination of the viscosity for clinical purposes is accomplished by the use of special forms of apparatus termed viscosimeters. These for the most part consist of capillary tubes through which distilled water and blood are caused to flow under the influence of a constant positive or negative pressure. The distance the water flows in a unit of time, compared with that of blood, represents the degree of viscosity. Among these apparatus those of Hess and Determann are generally employed, descriptions of which will be found in works on diagnosis.

8. **Coagulability.**—Within a few minutes after the blood is withdrawn from the vessels of a living animal it begins to lose its fluidity, becomes somewhat viscid, and if left undisturbed passes rapidly into a semisolid or jelly-like state. To this change in the physical condition of the blood the term coagulation has been applied. The blood, during the progress of coagulation, not only assumes the shape of the vessel in which it is contained, but becomes so firmly adherent to its walls that it may be inverted without the coagulum becoming dislodged. If a portion of such a jelly-like mass be examined microscopically, it will be found to be penetrated in all directions by a felt-work of extremely fine delicate fibrils, which, having made their appearance before the corpuscles have had time to settle to the bottom of the fluid, have entangled them in the meshes so that the entire mass retains its characteristic color. These fibrils are collectively known as fibrin (Fig. 92).

If the coagulated blood be allowed to remain undisturbed, a clear, transparent, slightly yellowish fluid makes its appearance on the surface of the mass, which as it accumulates forms a layer of varying degrees of thickness. Within a few hours the blood-mass detaches itself from the sides of the vessel in consequence of the retraction of the fibrils, while at the same time the clear fluid increases in amount and accumulates along the sides and bottom of the vessel. The shrinkage in the volume of the red coagulum and the increase of the volume of the clear fluid which is expressed from its meshes continue for a period varying from ten to fifteen hours, according to certain external conditions. The blood has now become separated into two distinct portions: viz.: a solid contracted red mass, termed *clot,* and a clear fluid, termed *serum.* The clot consists of the fibrin containing in its meshes the red and white corpuscles; the serum consists of all the constituents of the plasma except the antecedents of the fibrin. The stages of coagulation are shown in Fig. 92.

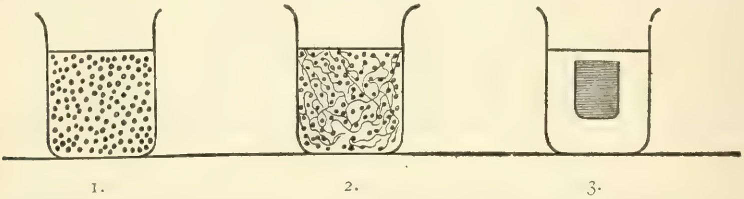

FIG. 92.—DIAGRAM TO ILLUSTRATE THE PROCESS OF COAGULATION. 1. Fresh blood, plasma and corpuscles. 2. Coagulating blood (birth of fibrin). 3. Coagulated blood (clot and serum).—(*Waller.*)

If the blood coagulates slowly the red corpuscles, owing to their greater specific gravity, subside to the bottom of the blood mass, giving to it a deeper color; the white corpuscles, owing to their lesser specific gravity, remain near the surface of the clot and give to it a more or less whitish appearance, producing the so-called *buffy coat.* In certain inflammatory conditions the coagulating power of the blood is much diminished, and the corpuscles, having time to subside, a well-developed buffy coat is formed which at one time had much interest for pathologists. As the contraction of the fibrin takes place more actively in the center, there being here less resistance than at the sides of the coagulum, the upper surface usually becomes depressed or cupped.

Coagulation of Plasma.—Clear plasma may be obtained by means of the centrifuge from blood to which sufficient magnesium sulphate has been added to prevent coagulation, or from horse's blood which has been allowed to flow into a tall vessel surrounded by a cooling mixture so as to prevent coagulation and thus permit the red corpuscles to subside. If such plasma is subjected to room-temperature, it very shortly undergoes coagulation, exhibiting practically the same phenomena as blood itself. After a variable length of time it also separates into a soft, colorless coagulum or clot consisting of fibrin, and a clear fluid, the serum. The presence of the red corpuscles is therefore not essential to the process of coagulation.

Rapidity of Coagulation.—The rapidity with which the blood coagulates varies in different classes of animals under the same conditions: *e.g.*, the blood of the pigeon coagulates immediately; that of the dog, in from one to three minutes; that of the horse, in from five to thirteen minutes; that of man, in from four to seven minutes. The time, however, can be lengthened or shortened by either changing the external conditions or by altering temporarily the normal composition of the blood.

Coagulation is retarded or prevented by the following agents, viz.: (1) A low temperature, especially that of melting ice. (2) The addition of magnesium sulphate (1 volume of a 25 per cent. solution to 3 volumes of blood); of sodium sulphate (1 volume of a saturated solution to 7 volumes of blood). (3) The addition of potassium oxalate (1 volume of a 1 per cent. solution to 3 volumes of blood). (4) The injection into the circulating blood of commercial peptone. (5) The mouth secretion of the leech.

Coagulation is hastened by the following agents, viz.: (1) a temperature gradually increasing from 38°C. to 50°C. (2) The addition of water in not too large amounts. (3) The presence of foreign bodies. (4) Agitation of the blood—*e.g.*, stirring.

Fibrin and Defibrinated Blood.—If freshly drawn blood is stirred with a bundle of twigs or glass rods for a few minutes, the fibrin collects on them in the form of thick bundles or strands; on washing it with water the entangled corpuscles are removed, when the fibrin assumes its natural white appearance. The strands can be resolved into a large number of delicate fibers which possess extensibility and retractility, and are therefore elastic. The chemic features of fibrin have already been considered (see page 19). The remaining fluid, similar in its physical appearance to the blood, is termed *defibrinated blood.* When such blood is allowed to remain at rest for a few days, the remaining red corpuscles gradually sink to the bottom of the fluid, above which will be found the clear serum.

CHEMIC COMPOSITION OF PLASMA AND SERUM

Plasma.—The plasma obtained by any of the methods previously described is a clear, colorless, transparent, slightly viscid fluid, with a specific gravity of 1.026 to 1.029. It is composed largely of water holding in solution proteins, sugar, fat, inorganic salts, urea, cholesterin, lecithin, etc. In composition it is quite complex, containing as it does not only the nutritive materials derived from the digestion of the food, but also the substances resulting from the disintegration of the tissues consequent on their functional activity.

Serum.—The serum is the clear, transparent, slightly yellow fluid expressed from the coagulated blood during the contraction of the fibrin. It consists practically of the ingredients of the plasma, with the exception of those substances which entered into the formation of fibrin.

The average composition of plasma is shown in the following table·

CHEMIC COMPOSITION OF PLASMA

Water		90.00
Proteins	Plasma-albumin	4.50
	Paraglobulin	3.40
	Fibrinogen	0.30
Fatty matters		0.25
Sugar		0.10
Extractives		0.60
Inorganic salts		0.85
		100.00

Plasma-albumin.—Of the protein constituents of the blood, plasma- or serum-albumin is the most abundant, existing to the extent of from 4 to 5 per cent. It is readily obtained from plasma or serum by saturating either of these fluids with magnesium sulphate, when all the proteins except serum-albumin are precipitated. After their removal the remaining fluid is subjected to a temperature of from 70° to 75°C., when the serum-albumin is precipitated in a coagulable form, after which it can be removed and its chemic features determined. Recent investigations indicate that plasma-albumin consists of, at least, more than one substance, since it can be separated into a crystallizable and non-crystallizable or an amorphous portion both of which however respond to the usual tests for albumin.

The origin and function of plasma-albumin are both obscure. Until quite recently it has been regarded, owing to its similarity to egg-albumin, and to its presence in the blood, as holding an important position as a nutritive agent. It was assumed that it originated in a synthesis of the products of protein digestion—peptones and amino-acids—in the epithelial cells covering the villi and by them discharged into the blood of the portal, and finally into the blood of the general circulation. On reaching the capillaries it was supposed to cross the endothelial wall, to become a constituent of the lymph and then to be utilized by the tissue cells for growth and repair. As was stated in the chapter on absorption, this view has been made untenable by reason of the apparent fact that the products of protein digestion—the amino-acids—are absorbed and enter the blood as such and carried direct to the tissue cells by which they are directly synthesized to the protein by which they are characterized. Plasma-albumin must therefore have, if this view prevails, some other origin and function. Future experimentation may disclose both.

Paraglobulin.—This protein, though present in plasma, is best obtained from serum when this fluid is saturated with magnesium sulphate. As the line of saturation is approached the fluid becomes turbid, and after a few minutes a fine white precipitate occurs. It can then be collected on a filter, dried, and its chemic properties determined. In its reactions it resembles the various members of the globulin class. The amount varies from 2 to 4 per cent. in the blood of man. As to the physiologic importance or antecedents of paraglobulin nothing is definitely known. Its constant presence in the blood would indicate that it plays an equally important, though perhaps different, part with serum-albumin in the nutrition of the body.

Fibrinogen.—This protein can be obtained from plasma, lymph, pericardial, and peritoneal fluids, as well as from hydrocele fluid. It is, however, not to be obtained from serum, as it is removed from the blood during the formation of solid fibrin. It is normally present in the blood in very small quantity, amounting to not more than 0.22 to 0.33 part per hundred. Fibrinogen may be obtained from plasma which has been prevented from coagulating, by the addition of magnesium sulphate in certain quantities or by the addition of a saturated solution of sodium chlorid. In a few minutes a flaky precipitate occurs. By repeated washing and precipitation with sodium-chlorid solutions of varying strength, the fibrinogen may be obtained in a pure state. The history of fibrinogen is unknown, though there is some experimental evidence for the belief that it is produced in the liver though out of what has not been determined. Beyond the fact that it contributes to the occasional formation of fibrin there is no positive knowledge either as to its origin, its nutritive value, or its final disposition in the blood under normal conditions.

Fat.—The plasma, and the serum as well, contains a very small quantity of fat in the form of microscopic globules. Though the percentage is normally not above 0.25, yet just after a meal rich in fat the amount may be so great as to give to the blood a milky or opalescent appearance. Within a few hours, however, this excess of fat disappears from the blood. As oxidation of fat in the blood has not been established the probabilities are that the microscopic granules pass across the walls of the capillaries and become constituents of the lymph. Soaps or alkaline salts of the fat acids, though formed during the digestion of fats, are not present in the blood. Lecithin and cholesterin are present in very small quantities.

Sugar.—The plasma also contains a small quantity of sugar in the form of dextrose and is to be regarded as a normal constituent. The percentage of the sugar varies from 0.10 to 0.20 per cent. To this condition of the blood in which the sugar is present in but normal amounts the term *glycemia* has been given. If the percentage falls below the normal amount, a condition of *hypoglycemia* is established; if on the contrary the percentage is increased beyond the normal a condition of *hyperglycemia* is established, whereupon the excess will be for the most part eliminated by the kidneys giving rise to a condition known as *glycosuria.*

If the statement be accepted that the amount of blood in a body weighing 70 kilos is 3864 grams (1/19th of the body weight) the amount of sugar in the entire volume of blood is at most about 7.72 grams, an amount which does not materially change under physiologic conditions.

Extractives.—The blood contains a series of nitrogenized bodies, such as urea, uric acid, creatin, creatinin, xanthin, etc., which result from the katabolic changes in nerve- and muscle-tissues as well as from subsequent chemic combinations and decompositions. Though constantly absorbed from the tissues, they seldom accumulate beyond a small amount, since they are constantly being eliminated from the blood by the various excretory organs.

Inorganic Salts.—The inorganic salts of the plasma are chiefly sodium and potassium chlorids, sulphates, and phosphates, together with calcium and magnesium phosphates. Of the salts, sodium chlorid is the most abundant, amounting to 0.56 part per hundred. Calcium phosphate is present in small quantity, 0.2 part per 100. This salt is not present to the same extent in serum for the reason that it became a constituent of fibrin at the time of coagulation. In other respects serum differs but slightly from plasma in the proportions of its saline constituents.

HISTOLOGY OF THE RED CORPUSCLES OR ERYTHROCYTES

The histologic features of the red corpuscles are readily observed in a drop of freshly drawn blood when examined microscopically. The field of the microscope will be seen to be crowded with red corpuscles floating in a clear transparent fluid—the plasma. Here and there will also be seen a white corpuscle, round or irregular in shape, and granular in appearance. Within a short time a characteristic phenomenon takes place: viz., the arranging of the corpuscles in the form of columns of varying lengths, resembling rolls of coins. These rolls interlace with each other at all angles and form a network in the meshes of which lie individual red and white corpuscles. (See Fig. 93.) The cause of this tendency of the corpuscles to adhere to one another is not definitely known. Since it does not take place in circulating blood, and since it is to a great extent prevented by defibrinating the blood, it has been supposed to be dependent on the formation of some adhesive substance connected with the formation of fibrin.

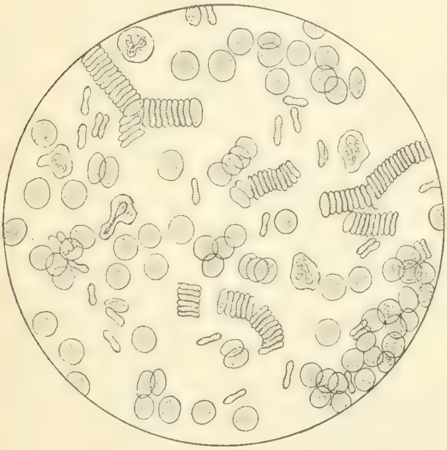

Fig. 93.—Corpuscles from Human Subject. A few colorless corpuscles are seen among the colored discs, many of which are arranged in rouleaux.—(*Funke.*)

Color.—When viewed by transmitted light, a single corpuscle is slightly yellow or greenish in color; but when a number are grouped together, the color deepens and the corpuscles appear red. In either case the color is due to the presence in the corpuscle of a specific coloring-matter, hemoglobin.

Shape.—The red corpuscle is a circular, flattened disc with rounded edges. Each surface is perfectly smooth and presents a shallow depression in its center, so that it is also biconcave. A longitudinal section of a corpuscle would present, when viewed edgewise, an outline similar to that of Fig. 94. This difference in the thickness of the peripheral and central portions of the corpuscle gives rise to differences in optical appearances when examined microscopically. At a certain distance of the object-glass the corpuscle presents in its peripheral portion a bright rim, and in its central portion a dark spot If the objective be brought nearer and the center accurately focused, the reverse appearance obtains; the central portion becomes bright and the peripheral portion dark. The cause of this difference in optical appearance is the unequal distribution of the transmitted light in consequence of the shape of the corpuscle.

Size.—The diameter of a typical well-developed red corpuscle under normal conditions is 0.0075 mm., its greatest thickness is 0.0019 mm. Though this may be assumed as the average diameter, there is a small percentage of distinctly smaller and a small percentage of distinctly larger corpuscles. The following table shows the results of measurements made by different observers:

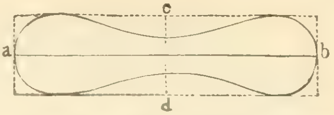

Fig. 94.—Ideal Transverse Section of a Human Red Corpuscle. (Magnified 5000 times.) *a*, *b*. Diameter. *c*, *d*. Thickness.

	Normal Limits.	Average Diameter.
Welcker	diameter 0.0045–0.0095 mm	0.0070 mm.
Hayem	diameter 0.0060–0.0088 mm	0.0075 mm.
Gram	diameter 0.0067–0.0093 mm	0.0078 mm.
Melassez		0.0076 mm.
		0.00747 ($\frac{1}{3200}$ inch)

Structure.—The red corpuscle of man as well as of all other mammals possesses neither a nucleus nor a limiting membrane, but appears to consist of a homogeneous substance more or less semisolid in consistence. Under the influence of certain reagents the corpuscle separates into two distinct portions: viz., a colorless protoplasmic stroma and a coloring-matter which diffuses into the surrounding liquid. The presence of the former can be demonstrated by the addition of iodin, which imparts to it a faint yellow color. The stroma is elastic, and determines not only the shape of the corpuscle but gives to it the properties of extensibility and retractility.

The foregoing is the classic and generally accepted view as to the shape, size, and structure of the red corpuscle. Nevertheless recent investigations render it probable that the statements were based on observations of the corpuscles under artificial rather than natural conditions, and therefore not strictly true. For many years histologists from time to time have stated that the red corpuscle is not circular and biconcave in shape, in the circulating blood, but bell-shaped, similar to that shown in Fig. 95. It was not until 1902, after the publication of Weidenreich's investigations, that this view began to receive more attention than had hitherto been accorded it. Weidenreich preserved in a moist chamber a hanging drop of human blood, and on examination found that the red corpuscles were bell-shaped though the depth of the bell cavity varied considerably. An examination of the capillary circulation in the omentum of the rabbit revealed the fact that the corpuscles in their natural medium were also bell-shaped. The circular biconcave shape they ordinarily present when a drop of blood is examined microscopically he attributes to cooling, evaporation and concentration of the drawn blood. Experimentally it was shown that when blood was added to 0.6 to 0.65 per cent. solution of sodium chlorid all the corpuscles were bell-shaped, but if the solution was increased or decreased in strength, this form was at once changed.

The dimensions of the bell-shaped cell according to Weidenreich are as follows:—

Greatest diameter	7 microns	0.007 mm.
Diameter of cavity	3 microns	0.003 mm.
Height of bell	4 microns	0.004 mm.
Height of cavity	2.5 microns	0.0025 mm.
Thickness of wall at apex	2 microns	0.002 mm.
Thickness of wall at base	1.5 microns	0.0015 mm.

The foregoing observations have been confirmed by many subsequent investigators. Thus Lewis states that if a drop of blood is placed immediately on a warm slide and examined, the corpuscles exhibit the bell shape, but as the slide cools they gradually become biconcave discs of the conventional form. He also observed that the corpuscles in the capillary blood-vessels of the omentum of the guinea-pig were bell-shaped and presenting an appearance similar to that shown in Fig. 95. Radasch found on examination of fetal tissues such as the spleen, kidney, liver, placenta, etc., that the great majority of the corpuscles in all situations presented the bell shape rather than the circular biconcave shape. This observer is of the opinion that the bell shape can not be due to the action of the fixatives employed in the preparation of the tissues.

The structure of the corpuscle, according to Weidenreich, differs also from that usually stated. He asserts that the corpuscle is surrounded by a structureless, colorless membrane enclosing a colored but not nucleated semi-fluid mass, which consists chemically of protein material, lecithin, cholesterin, inorganic salts and hemoglobin. There is no evidence of the existence of a stroma in the adult state.

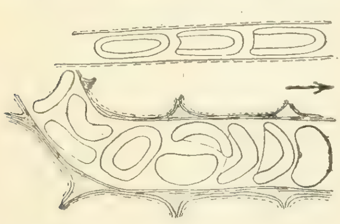

FIG. 95.—RED CORPUSCLES SKETCHED WHILE CIRCULATING IN THE VESSELS OF THE OMENTUM OF A GUINEA-PIG. (*F. T. Lewis in Stöhr's Histology.*)

Number of Red Corpuscles.—In any given specimen of blood the corpuscles are so numerous and the spaces between them so small that it seems almost impossible to determine their number. This, however, has been accomplished for a cubic millimeter of blood by various observers employing different methods with comparatively uniform results. The average normal number of corpuscles in one cubic millimeter of blood is, for men, 5,000,000; and for women, 4,500,000. This value, however, will vary within slight limits, with variations in the activity of physiologic processes and to a large extent at times in pathologic states of the blood or body. The number is increased in the cutaneous veins by all influences which cause a diminution in the quantity of water in the blood—*e.g.*, copious sweating, acute watery diarrhea, fasting, abstinence from liquids; the number is diminished by influences which dilute the blood—*e.g.*, the ingestion of liquids, the absorption of fluids from the tissue spaces, etc. But it is well to remember that these influences which produce changes in the number of corpuscles per cubic millimeter do not necessarily produce corresponding changes in the total number of red corpuscles in the body. In women lactation, menstruation, and the act of parturition diminish the number. High altitudes apparently increase the number of corpuscles, as shown by their increase in the blood of the peripheral vessels. Whether this is an indication that there is a corresponding increase of the total number in the general volume of the blood is uncertain. The following table will show the increase in the count per cubic millimeter at different altitudes:

Place	Height Above Sea-level	Red Cells	Author
Christiania	0 meter	4,974,000	Laache.
Göttingen	148 meters	5,225,000	Schaper.
Tübingen	314 meters	5,322,000	Reinert.
Zürich	414 meters	5,752,000	Steirlin.
Auerbach	425 meters	5,748,000	Köppe.
Reibaldsgrün	700 meters	5,900,000	Köppe.
Arosa	1800 meters	7,000,000	Egger.
The Cordilleras	4392 meters	8,000,000	Viault.
			(Köppe.)

This increase in the number of corpuscles takes place, according to Viault's observations, within two or three weeks, and is apparently not connected with either diet or mode of life, but rather with diminished atmospheric, if not oxygen, pressure. On returning to sea-level there is a gradual reduction, without any apparent destruction of the corpuscles, to their normal number. The reason for these variations is not clear.

The method of counting corpuscles introduced by Vierordt and Welcker has been modified by different observers, and especially by Thoma. On account of the great number of corpuscles in 1 cubic millimeter of blood, it becomes necessary for purposes of enumeration that the blood be diluted a definite number of times and that the diluted mixture be placed in a counting chamber possessing a definite capacity. By means of the pipette or *mélangeur* of Potain and the counting chamber of Thoma both these objects are attained.

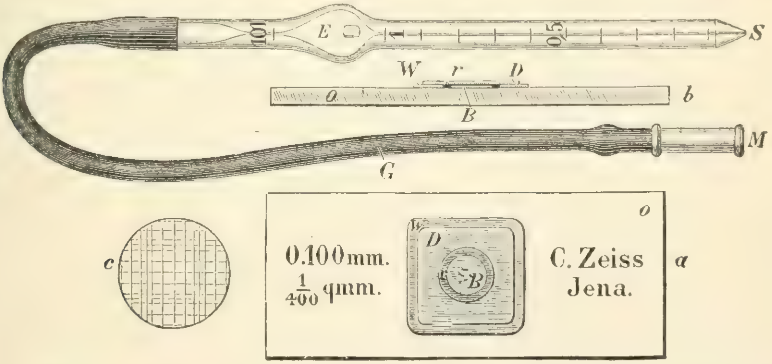

FIG. 96.—HEMOCYTOMETER. *a*, Surface; *b*, section view; *c*, squares on the surface of *B* magnified. *M*, *G*, *S*, mouth piece, rubber tube and pipette.

The pipette consists of a capillary tube (Fig. 96) provided with an enlargement containing a freely movable small glass ball, E. One end of the tube, S, is pointed, while to the other end is attached a rubber tube, G, for the purpose of facilitating the introduction of the blood and the diluting fluid. The capillary tube, which is accurately calibrated, carries marks, 0.5, 1, 101, which signify that if the tube be filled with blood up to the mark 1 and the diluting fluid be sucked into the tube up to the mark 101, the blood will be diluted 100 times. If the blood be sucked up to the mark 0.5 and the diluting fluid to 101, then the blood will be diluted 200 times. In using the pipette the point is introduced into a drop of blood derived from a small wound in the skin of the lobe of the ear or finger and sucked into the tube by introducing the end, M, of the rubber tube into the mouth. The tube is then quickly inserted into a solution which will preserve the shape and size of the corpuscles, such as Gowers's sodium sulphate solution, sp. gr. 1.025, or a 3 per cent. sodium chlorid solution,[1] and the fluid sucked into the tube up to the mark 101. On shaking the pipette for a few minutes, the admixture will take place, aided by the movements of the glass ball.

Fig. 96 shows both a surface view, a, and a section view, b, of the counting chamber. This consists of an oblong glass plate, o, on which are cemented two small pieces of glass, one of which, WD, has in the center a circular opening in which is placed the other, B, a circular disc or stage. Their relation is such that a narrow groove or moat separates the one from the other, the floor of which is formed by the glass plate. The surface of the circular stage is exactly 0.1 mm. lower than that of the cover-glass, r. On the surface of the glass stage a series of small squares is engraved, C, each one of which has a side length of $\frac{1}{20}$ mm. and an area of $\frac{1}{400}$ square mm. To facilitate counting, a group of 16 such squares is surrounded by a thick line. Fig. 97. This group is separated from adjoining groups, also enclosed by thick lines, by an intermediate fine line, which serves as a guide in passing from one group to another. When a cover-glass is accurately applied to the glass, b, each one of the small squares will have a cubic capacity of $\frac{1}{400}\times 0.1$, or $\frac{1}{4000}$ cubic millimeter.

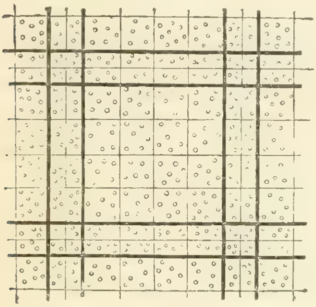

Fig. 97.—Microscopic Appearance of the Small Squares and the Distribution of the Corpuscles.

Before placing the diluted blood on the counting stage, the fluid in the tube of the pipette should be blown out and discarded, as it contains no portion of the blood. A small drop is then placed on the glass stage and covered with the cover-glass. After a few minutes the corpuscles settle upon the ruled spaces and are ready for counting. The number of corpuscles in at least five series of sixteen small squares is then counted; this number is then multiplied by the degree of dilution (100 or 200 as the case may be) and this divided by the cubic contents of each small square ($\frac{1}{4000}$); the product is then divided by the number of squares counted (80 in the instance given above): *e.g.*, five series of sixteen small squares contain 500 corpuscles

$$\frac{500\times200\times4000}{80}=5{,}000{,}000 \text{ erythrocytes per c.mm.,}$$

The accuracy of the counting is proportional to the number of squares counted. If 200 squares are counted with each of two different drops, and the average taken the probable limit of error will be less than 2 per cent.

The Preservation of the Red Corpuscles in the Plasma.—Within the blood-vessels the physical conditions and chemic composition of the plasma are such that both the form, and the composition of the corpuscle or the relation of the hemoglobin to the stroma, are maintained in the normal or physio-

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[1] Various solutions have been devised for diluting blood, any one of which may be employed, *e.g.*:

Hayem's Fluid:

Hydrarg. bichlor	0.5 gm.
Sodii sulphat	5.0 gm.
Sodii chlorid	2.0 gm.
Aquæ destillat	200.0 gm.

Toisson's Fluid:

Aquæ destillat	160.00 parts.
Glycerinæ	30.00 parts
Sodii sulphat	8.00 parts.
Sodii chlorid	1.00 part.
Methyl-violet	0.025 part.

Gower's Fluid:

Sodii sulphat	gr. 104
Acid. acetic	ʒj
Aquæ dest	q. s. ad ℥iv.

logic condition. The plasma is preservative of the structure and function of the corpuscle. The reason assigned for this is that the osmotic pressure of the salts in the plasma and of the salts in the corpuscle exactly balance one another so that there is neither an absorption of water from, nor a yielding of water to the plasma, on the part of the corpuscle. The plasma having an osmotic pressure equal to that within the corpuscle is said to be *isotonic* with it.

When blood is to be prepared for microscopic examination with a view of determining the histologic features of the corpuscles or for purposes of enumeration, it must be diluted, and unless special precautions are observed the condition of equal osmotic pressure will be disturbed by the diluting agent and the corpuscles will lose their characteristic form and structure from either an absorption or loss of water.

If distilled water is employed for this purpose, the osmotic pressure of the plasma is of course diminished, and in consequence the osmotic pressure of the inorganic constituents of the corpuscles (particularly potassium phosphate) causes an inflow of water. The corpuscle therefore swells and assumes a more or less spheric form; the hemoglobin is dissociated and discharged into the surrounding fluid throughout which it diffuses. Such an environment having an osmotic pressure less than that of the corpuscle is said to be *hypotonic*, *hypisotonic*, or *hypo-isotonic* to it.

If on the contrary, water containing inorganic salts (particularly sodium chlorid) is added in amounts which impart to the plasma an osmotic pressure greater than that within the corpuscle, there will be an outflow of water from the corpuscle, a shrinkage of the volume and a crenation of its surface. Such an environment having an osmotic pressure greater than that of the corpuscle is said to be *hypertonic*, or *hyperisotonic* to it. It is essential therefore in diluting the plasma with water, that the latter contains inorganic salts in such amounts that the resulting mixture (plasma and water) possesses an osmotic pressure equal to that of the original plasma or to that of the corpuscle. A diluting agent well adapted for this purpose is the well-known Ringer's mixture. Other solutions which preserve the form of the corpuscles during the time required for their enumeration are the solutions devised by Hayem, Toisson, and Gowers alluded to on a preceding page. Because of the fact that sodium chlorid is the chief inorganic constituent of the plasma it is common in laboratory work to dilute the plasma of mammalian blood and of frog's blood with solutions of sodium chlorid of 0.9 per cent. and 0.6 per cent. respectively, which though not absolutely are sufficiently isotonic for the purpose desired.

The Effects of Reagents.—Many other saline solutions with an osmotic pressure greater or less than normal plasma, dilute solutions of acids and alkalies, bile salts, chloroform, ether, ammonium sulphocyanid, electricity, etc., also destroy the physical and chemic integrity of the corpuscle and cause the hemoglobin to separate from the stroma and diffuse into the plasma without itself undergoing any appreciable change in composition. With the escape and diffusion of the hemoglobin the blood becomes transparent and changes to a dark red color to which the term "laky" has been given. The mechanism by which the hemoglobin becomes dissociated and discharged from the corpuscle by these agents is unknown. The disintegration of the corpuscle and the diffusion of the hemoglobin into, and its solution by the surrounding medium, is termed *hemolysis* and the agents by which it is produced are termed *hemolytic* agents.

CHEMIC COMPOSITION OF RED CORPUSCLES

When analyzed chemically the red corpuscles are found to consist of water 65 per cent. and solid matter 35 per cent. The solids, moreover, have been found to consist of a pigment hemoglobin 33, protein 0.9, cholesterin and lecithin 0.46, and inorganic salts (chiefly potassium phosphate and chlorid and sodium chlorid) 1.4 per cent. respectively. Of the total solids the hemoglobin constitutes about 94 per cent.

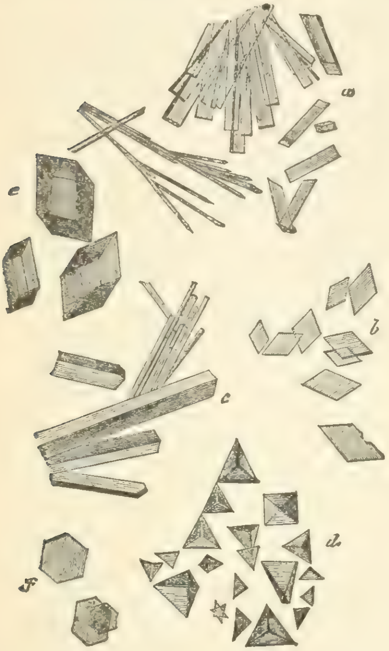

FIG. 98.—CRYSTALLIZED HEMOGLOBIN. *a*, *b*. Crystals from venous blood of man. *c*. From blood of cat. *d*. Of guinea-pig. *e*. Of marmot. *f*. Of squirrel.—(*Gautier.*)

Hemoglobin.—In the normal condition of the corpuscle the hemoglobin is in an amorphous condition and is combined in some unknown way with the stroma.

When hemoglobin is decomposed in the absence of oxygen it undergoes a cleavage into a protein, globin, and an iron-holding pigment, hemochromogen, which constitutes about 4 per cent. of the molecule. If a solution of hemochromogen be exposed to air it absorbs oxygen and is converted into hematin. This latter compound can also be derived directly from hemoglobin by the action of acids and alkalies. It is to the presence of hemochromogen in combination with the protein globin that the hemoglobin is indebted for its power of absorbing and carrying oxygen.

If blood which has been rendered laky, by water or any other of the known agencies, be allowed to evaporate slowly, the dissolved hemoglobin undergoes crystallization. The rapidity with which the crystals form varies in the blood of different animals under similar conditions. According to the ease with which crystallization takes place, Preyer has classified various animals as follows: (1) Very difficult—calf, pigeon, pig, frog; (2) difficult—man, monkey, rabbit, sheep; (3) easy—cat, dog, mouse, horse; (4) very easy—guinea-pig, rat.

The hemoglobin crystals vary in shape according to the blood from which they are obtained (Fig. 98). Those obtained from the guinea-pig are tetrahedral; those from man and most mammals are prismatic rhombs; those from the squirrel are in the form of hexagonal plates. Notwithstanding these slight differences, all forms belong to the same crystal system, with the exception of those from the squirrel.

A simple but very effective method of obtaining blood-crystals suggested by Reichert is to lake defibrinated blood, especially that of the dog, rat, guinea-pig, and horse, with acetic or ethylic ether and then add a solution, 1 to 5 per cent., of ammonium oxalate. A drop of this mixture placed under the microscope will show crystal formation in a very few minutes.

Chemic Composition of Hemoglobin.—By appropriate methods hemoglobin can be obtained in a practically pure form, and when subjected to a temperature of 100°C. its water of crystallization is driven off, after which it can be analyzed. In the subjoined table the results of several analyses are given for 100 parts of hemoglobin.

	Dog	Horse	Dog	Guinea-pig
C....................	53.91	51.15	53.85	54.12
O....................	22.62	23.43	21.84	20.68
H....................	6.62	6.76	7.32	7.36
N....................	15.98	17.94	16.17	16.78
S....................	0.54	0.39	0.39	0.58
Fe....................	0.33	0.33	0.43	0.48
	Jaquet.	Zinoffsky.	Hoppe-Seyler.	

The percentage composition of hemoglobin is thus seen to vary slightly in different animals, suggesting that there may be different kinds of hemoglobin. The molecular composition is not known. On the assumption that each molecule contains one atom of iron, Preyer suggested the following empirical formula: $C_{600}H_{960}N_{154}O_{179}S_3Fe$, with a molecular weight of 13,332; Jaquet has suggested a different formula: $C_{758}H_{1203}N_{195}O_{218}S_3Fe$, with a molecular weight of 16,669. It is very evident from this that the molecule is of enormous size and exceedingly complex.

Quantity of Hemoglobin.—The quantity of hemoglobin in blood as determined by chemic, chromometric, and spectro-photometric methods amounts to about 14 per cent. in man and 13 per cent. in woman. Of the chemic methods, that based on the amount of iron is the one generally employed. Chemic analysis has shown that hemoglobin contains 0.33 per cent. and blood 0.046 per cent. of iron; with these two factors the quantity of hemoglobin can be determined by the following formula: $x=\frac{100\times0.046}{0.33}=$ 14 per cent. The total quantity of hemoglobin in the blood, assuming the latter to be about 3684 grams (one-nineteenth of the body-weight, 70 kilos) will therefore amount to 515 grams; *e.g.*, $x=\frac{3684\times14}{100}=515$. The total amount of iron in the blood is obtained by the following formula: viz., $x=\frac{3684\times0.046}{100}=1.70$ grams.

Clinic Methods for the Determination of the Percentage of Hemoglobin.—Under normal physiologic conditions the percentage of hemoglobin undergoes but slight variation. In pathologic states there is frequently a great diminution in the amount, especially in chlorosis, splenic leukemia, and pernicious anemia, diseases in which it diminishes to a considerable per cent. in many instances. For clinic purposes it becomes a matter of importance to have some method by which the diminution of hemoglobin can be determined. In the various methods employed the normal amount of hemoglobin is considered as 100 per cent. and the normal number of red corpuscles, 5,000,000 per cubic millimeter, is also considered as 100 per cent. Under such conditions the corpuscles have a normal color known as the *color index*. This is expressed by a fraction of which the percentage of hemoglobin is the numerator and the percentage of corpuscles the denominator. The normal color index is therefore 1 or unity. In some pathologic states the hemoglobin alone diminishes, the number of the corpuscles remaining the same; in this instance the color index is less than unity, *e.g.*, if the hemoglobin be reduced to 80 per cent., as determined by the method to be described, then the color index will be $\frac{80}{100}=0.8$ which indicates that each corpuscle retains but eight-tenths of the normal amount of hemoglobin, or stated in the reverse way, each corpuscle has lost two-tenths of the normal amount of its hemoglobin. In other pathologic states there is both a diminution in the percentage of the hemoglobin and in the percentage of the corpuscles and the diminution may be equal or unequal in degree. If the diminution be equal the color index is unity; if it be unequal the color index is less or greater than unity; *e.g.*, if the percentage of hemoglobin be but 60 and the percentage of red corpuscles, as determined by the method of counting be but 80 (4,000,000 per cubic millimeter) then the color index is $\frac{60}{80}=0.75$ which indicates that each corpuscle retains but three-fourths of the normal amount of hemoglobin; if on the contrary the percentage of hemoglobin be but 60, and the percentage of red corpuscles be but 50 then the color index is 1.2 which indicates that each corpuscle contains a larger percentage of hemoglobin than normally. This condition is sometimes observed in pernicious anemia.

For the determination of these variations in the hemoglobin for clinical purposes two chromometric methods are at present largely employed, that of Gowers and v. Fleischl. All chromometric methods are based on the principle that if two equally thick and equally well-illuminated solutions present the same intensity of color, their richness in coloring-matter is the same. There are two methods by which this can be done: (1) By diluting the blood to be examined with water until the shade of color corresponds to that of a solution of hemoglobin of known strength (Gowers). (2) Diluting a given quantity of blood with a given quantity of water and then finding an identical color which represents a previously determined quantity of hemoglobin (v. Fleischl).

Gowers' hemoglobinometer consists of two glass tubes of exactly the same size and similar to those shown in Fig. 99. One, A, contains glycerin jelly colored with picro-carmine the shade of which corresponds to that of normal blood diluted 100 times (20 c.mm. in 2000 c.mm. of water), representing a 1 per cent. solution. The other tube, B, is ascendingly graduated with 120 divisions, each one of which corresponds to 20 c.mm. With a graduated pipette, D, 20 cubic millimeters of blood are accurately measured and dropped into the bottom of the tube B, in which a few drops of distilled water have been placed so as to prevent coagulation. Water is then added drop by drop until the color of the diluted blood is exactly that of the standard. The division of the scale reached by the dilution will represent the relative percentage of hemoglobin. If this tint is not obtained until the dilution reaches 100 divisions, the quantity of hemoglobin is normal. If more water must be added, it is in excess; if less, it is diminished. If, for example, the 20 cubic millimeters of blood from an anemic patient gave the standard tint at 60 divisions, the blood contained but 60 per cent. of the normal amount of hemoglobin.

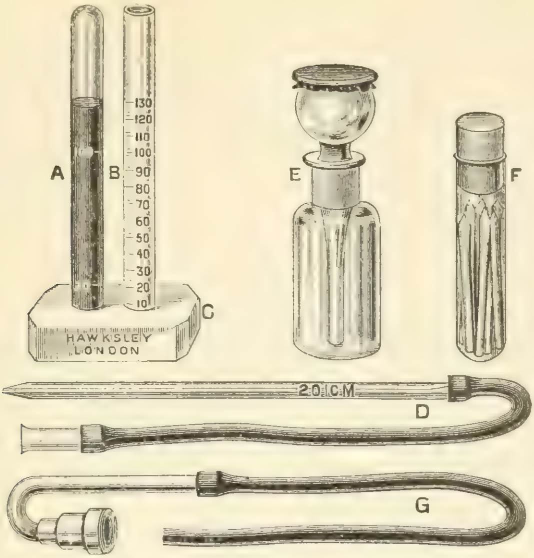
A
B
130
120
110
100
90
80
70
60
50
40
30
20
10
C
HAWKSLEY
LONDON
E
F
20 C.M
D
G

Fig. 99.—Haldane's Modification of Gowers' Apparatus.

Haldane's Modification of Gowers' Method.—Haldane's hemoglobinometer, Fig. 99, is a modification of that of Gowers. The tube A contains also a 1 per cent. solution of blood having the normal percentage of hemoglobin saturated with carbon monoxid. With the graduated capillary pipette, D, 20 cubic millimeters of blood are then obtained from a slight

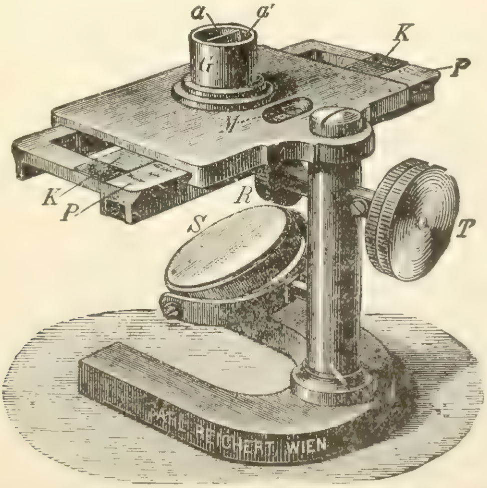
a
a'
K
P
G
M
K
P
R
S
T
CARL REICHERT WIEN

Fig. 100.—Von Fleischl's Hemometer. K. Red colored wedge of glass moved by R. G. Mixing vessel with two compartments, *a* and *a'*. M. Table with hole to read off the percentage of hemoglobin on the scale P. T. Pinion to move K. S. Mirror of plaster-of-Paris.

wound in the finger or elsewhere and then dropped into the tube B, in which a small quantity of distilled water from E was previously placed to prevent coagulation. The cap of G is then attached to a gas burner, through which flows either pure CO or a gas containing CO and the rubber tube inserted into D to the level of the water. After the gas has been flowing for a few seconds the rubber tube is withdrawn, and while the glass tube is yet full of the gas, it is closed with the thumb and gently shaken so as to convert all the hemoglobin into carbon-monoxid hemoglobin. This is then diluted very gradually as in the employment of the Gowers apparatus until the tint of the solution in B corresponds to that in A. The level at which this is observed indicates the percentage of hemoglobin in the blood used. The error in this method scarcely exceeds 1 per cent.

Von Fleischl's hemometer consists of a metallic cell divided into two compartments, a and a′, by a vertical partition (Fig. 100). In the former a definite quantity of blood is placed and diluted with a known quantity of water. Beneath the compartment a′ is placed a glass wedge stained with the golden purple of Cassius or similar pigment, the color of which passes from a deep red at one end to clear glass at the other (Fig. 101). To the side of this wedge is placed a scale ranging from 0 to 120. By means of the screw, R T, the glass wedge is moved until the color of the glass and diluted blood is identical. The illumination of the blood and glass wedge is accomplished by lamp-light reflected from the white reflecting surface beneath. The depth of color of the glass opposite 100 on the scale corresponds to that of normal blood. If, therefore, the colors are identical at 75 divisions, the blood contains but 75 per cent. of the normal amount of hemoglobin.

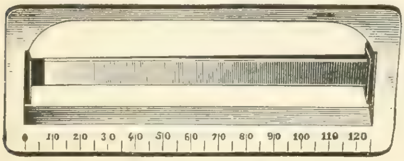

FIG. 101.—TINTED GLASS WEDGE OF THE VON FLEISCHL HEMOMETER.

Absorption Spectra.—Both oxyhemoglobin and reduced hemoglobin, like other soluble pigments, have an absorbing influence on certain waves of light, and hence give rise to absorption bands which can be studied with the spectroscope, and which are so characteristic as to serve for their identification.

In principle a spectroscope consists of a prism which decomposes the light from a narrow slit into a band of all the spectral colors. A form of spectroscope in common use is that shown in Fig. 102. It consists of a tube, B, which has at one end a slit that can be narrowed or widened by means of a screw. The light, having passed through it, falls on an achromatic convex lens (called the collimator) at the opposite end of the tube which renders the divergent rays of light parallel. These parallel rays subsequently fall on the prism, by which they are dispersed and directed into the tube, A, which is nothing more than a small telescope. On looking into it at the ocular end the spectral colors are seen. If the light has been derived from the sun, the spectrum will present vertical dark lines, the so-called Fraunhofer's lines. They are given from A to F in Fig. 103. If a colored medium be held in front of the slit so that the light has to pass through it first, certain dark bands will appear in the spectrum, owing to the absorption of certain rays.

Dilute solutions of arterial blood show absorption bands between the Fraunhofer lines, D and E, in the green and yellow portion of the spectrum.

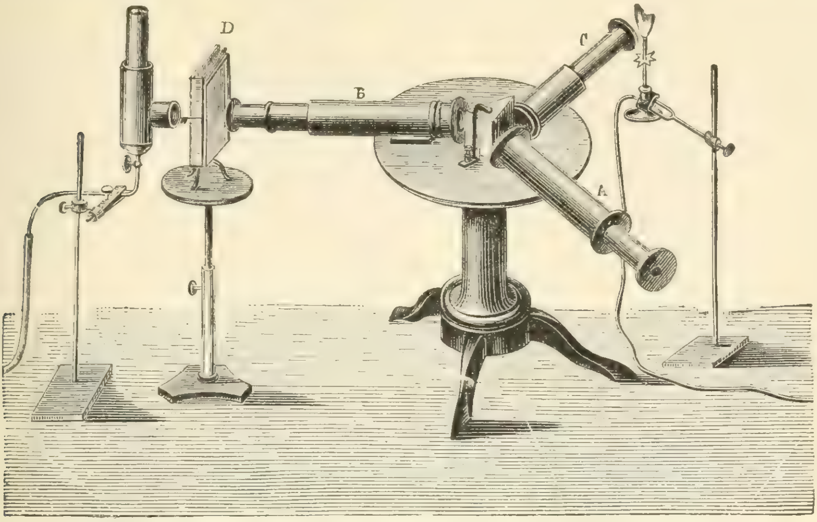

FIG. 102.—THE SPECTROSCOPE. A. Telescope. B. Tube for the admission of light and carrying the collimator. C. Tube containing a scale, the image of which when illuminated is reflected above the spectrum. D. The fluid examined.—(*Landois and Stirling.*)

(See Fig. 103.) The band nearest D, frequently designated as alpha, is dark in the center and sharply defined. The band which lies toward E, designated as beta, is broader and less sharply defined.

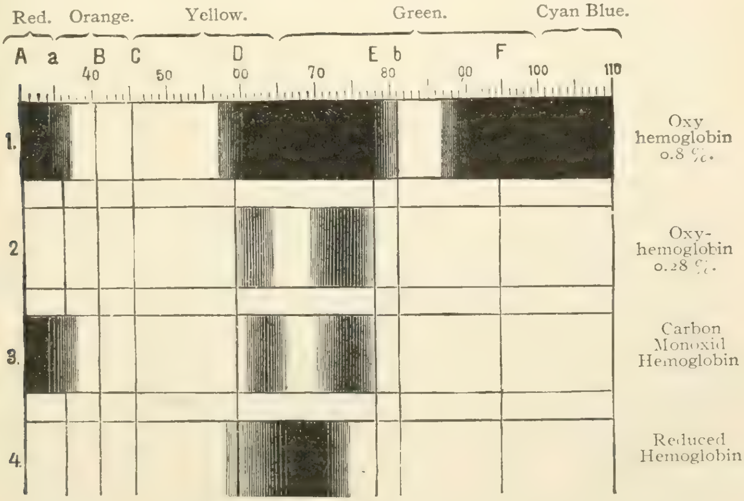
Red.
Orange.
Yellow.
Green.
Cyan Blue.
A
a
B
C
D
E
b
F
40
50
60
70
80
90
100
110
1.
2
3.
4.
Oxy hemoglobin 0.8 %.
Oxy-hemoglobin 0.28 %.
Carbon Monoxid Hemoglobin
Reduced Hemoglobin

FIG. 103.—SPECTRA OF HEMOGLOBIN AND SOME OF ITS COMPOUNDS. —(*Landois and Stirling.*)

As the amount of light absorbed varies with the concentration of the solution as well as its thickness, and gives rise to absorption bands of different widths and intensities, it becomes necessary, in order to obtain the characteristic bands, to employ only dilute solutions.

The absorption spectra, as seen with different strengths of solution one centimeter thick, are shown graphically in Fig. 104. It will be observed that solutions varying in strength from 0.1 per cent. to 0.6 per cent. give rise to the two characteristic bands, but with gradually increasing breadths. With a percentage greater than 0.65 per cent. the light between D and E, the yellow-green, becomes extinguished and the two bands fuse together, forming a single band overlapping slightly the lines D and E. At the same time there is a progressive darkening of the violet end of the spectrum. At 0.85 per cent., all the light is absorbed with the exception of a small amount of the red. Solutions less than 0.01 per cent. to 0.003 per cent. show but a single absorption band—that nearest D.

A solution of venous blood or of reduced hemoglobin shows but a single absorption band (see Fig. 103), frequently designated as gamma, broader and less marked between the lines D and E, but extending slightly beyond D. Fig. 105 shows in the same graphic manner the increasing breadth of the absorption band with increasing strengths of solution, as well as the simultaneous absorption of light at both the red and violet ends of the spectrum.

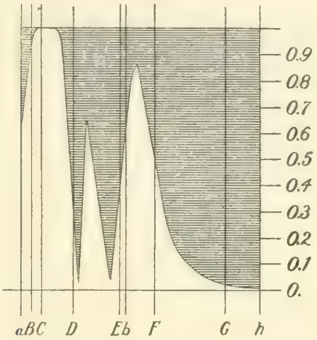

FIG. 104.—GRAPHIC REPRESENTATION OF THE ABSORPTION OF LIGHT IN A SPECTRUM BY SOLUTIONS OF OXYHEMOGLOBIN OF DIFFERENT STRENGTHS. The shading indicates the amount of absorption of the spectrum, and the numbers at the side the strength of the solution. —(*Rollet.*)

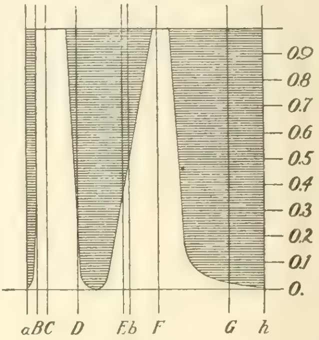

FIG. 105.—GRAPHIC REPRESENTATION OF THE ABSORPTION OF LIGHT IN A SPECTRUM BY SOLUTIONS OF REDUCED HEMOGLOBIN OF DIFFERENT STRENGTHS. The shading indicates the amount of absorption of the spectrum, and the numbers at the side the strength of the solution.—(*Rollet.*)

Oxyhemoglobin; Reduced Hemoglobin.—The coloring-matter of the blood is characterized by the property of combining with and of again yielding up oxygen. The union is a chemic one, taking place under certain pressure conditions. It therefore may exist in two states of oxidation, distinguished by a difference in color and their absorption spectra. If hemoglobin either in blood or in solution be shaken with air, it at once combines with oxygen and is converted into *oxyhemoglobin*, which imparts to the blood or solution a bright red or scarlet color. If the blood or solution be now deprived of oxygen, the oxyhemoglobin is converted into *reduced hemoglobin*, which imparts to the blood or solution a dark bluish-red or purple color.

The quantity of oxygen absorbed by 1 gram of hemoglobin is estimated at 1.56 c.c. measured at 0°C. and 760 mm. of mercury. The compound formed by the union of oxygen and hemoglobin is a very feeble one; for when the pressure is lowered the union becomes less stable, and as the zero point is approached, as in the Torricellian vacuum, a rapid dissociation of the oxygen takes place. This, however, is not due entirely to a fall of pressure but partly to the dissociation force of heat, which increases in power as the pressure falls. The same dissociation of oxygen can be brought about by passing through blood indifferent gases, such as hydrogen, nitrogen, carbon dioxid, which lower oxygen pressure, or by the addition of reducing agents, such as ammonium sulphid or Stokes' fluid.

These experimental determinations of the relation of oxygen to hemoglobin partly explain the oxidation and deoxidation of the hemoglobin in the lungs and tissues. As the blood passes through the lungs and is subjected to the oxygen pressure there, the hemoglobin combines with a definite quantity of oxygen, and on emerging from the lungs exhibits a bright red or scarlet color; as the blood passes through the systemic capillaries where the oxygen pressure in the surrounding tissues is low, the oxyhemoglobin yields up a portion of its oxygen, becoming deoxidized or reduced, and the blood on emerging from the tissues exhibits a dark bluish color. The portion of oxygen given up to the tissues is termed respiratory oxygen. In 100 parts of arterial blood the coloring-matter presents itself almost exclusively in the form of oxyhemoglobin. In passing through the capillaries about 5 per cent. only gives up its oxygen and becomes reduced, so that both kinds are present in venous blood. In asphyxiated blood only reduced hemoglobin is present. It is this capability of combining with and of again yielding up oxygen, that enables hemoglobin to become the carrier of oxygen from the lungs to the tissues.

Carbon Monoxid Hemoglobin.—Carbon monoxid is a constituent of coal-gas and more largely of water-gas. From either source it is likely to accumulate in the air, and if inspired for any length of time produces a series of effects which may eventuate in death. If blood be brought into contact with this gas, it assumes a bright cherry-red color, which is quite persistent and due to the displacement of the loosely combined oxygen and the union of the carbon monoxid with the hemoglobin. The compound thus formed is very stable and resists the action of various reducing agents. The passage of air or of some neutral gas through the blood for a long period of time will gradually displace the carbon monoxid and enable the hemoglobin again to absorb oxygen. It is for this reason that partial poisoning with the gas is not fatal. It is to its power of displacing oxygen and forming a stable compound with hemoglobin and thus interfering with its respiratory function that carbon monoxid owes its poisonous properties. Examined spectroscopically, solutions of carbon monoxid hemoglobin exhibit two absorption bands closely resembling in position and extent those of oxyhemoglobin; but careful examination shows that they are slightly nearer the violet end of the spectrum and closer together. (See Fig. 103.) A useful test for CO blood is the addition of caustic soda, which produces a cinnabar red precipitate.

Carbo-hemoglobin.—When hemoglobin is exposed to an atmosphere of oxygen and carbon dioxid, it will absorb the latter as well as the former, though the union of the oxygen under such circumstances is not as strong as when oxygen alone is present. To the compound formed by the union of the carbon dioxid and the hemoglobin the name carbo-hemoglobin has been given. The union, however, is not very stable as the carbon dioxid can be readily dissociated. As the carbon dioxid absorption will take place, even though the hemoglobin is practically saturated with oxygen, the assumption has been made that the oxygen combines with hemochromogen, and the carbon dioxid with the protein constituent—globin. If this be the case the hemoglobin and hence the red corpuscle, can be regarded as concerned in the absorption and transmission of carbon dioxid from the tissue to the lungs.

Methemoglobin.—This is a pigment, closely related to oxyhemoglobin, found in the blood after the administration of various drugs, in cysts and in the urine in hematuria and hemoglobinuria. It is also produced when a solution of hemoglobin is exposed to the air and becomes acid in reaction and brown in color. The spectrum shows two absorption bands similar to oxyhemoglobin, but in addition a new and quite distinct band near the line C, in the red. If the acid solution be rendered alkaline by the addition of ammonia, this band disappears and another makes its appearance near the line D. The addition of ammonium sulphid develops reduced hemoglobin, which, on the absorption of oxygen, produces again oxyhemoglobin, as shown by the spectroscope.

Hematin.—Boiling hemoglobin or adding to it acids or alkalies decomposes it and develops one or more protein bodies to which the general term globulin has been given, and an iron-holding pigment termed hematin. This is regarded as an oxidation product of hemoglobin and constitutes about 4 per cent. of its composition. When obtained in a pure state, it is a non-crystallizable blue-black powder with a metallic luster. According as it is treated with acids or alkalies, two combinations of hematin can be obtained (acid and alkaline), each of which has special properties, giving rise to different absorption bands.

Hemin.—This pigment is a derivative of hematin, presenting itself in the form of microscopic rhombic plates or rods (Teichmann's crystals), which are so characteristic as to serve as tests for blood-stains in medicolegal inquiries. These crystals are readily obtained by adding to a small quantity of dried blood on a glass slide a few drops of glacial acetic acid and a crystal of sodium chlorid; after heating gently for a few minutes over a spirit lamp and then allowing the mixture to cool, crystallization of the hemin soon takes place.

Hematoidin.—This term has been applied to a pigment which occurs in the form of yellow crystals in old blood-clots or in blood which has been extravasated into the tissues. In its chemic composition and in its reactions it closely resembles bilirubin, the pigment of the bile, exhibiting the same characteristic play of colors on the addition of nitric acid.

The Stroma.—The stroma of the red corpuscles obtained by the methods which dissolve out the hemoglobin has been shown by analysis to consist of from 60 to 70 per cent. of water and 40 to 30 per cent. of solid material, containing a proteid resembling cell-globulin, lecithin, cholesterin, and inorganic salts, among which potassium phosphate is especially abundant.

Life-history of Red Corpuscles.—In the performance of their functions the red corpuscles undergo more or less disintegration and finally destruction; but as the average number is maintained under normal physiologic conditions, there must be a constant renewal of corpuscles from day to day. The evidence of destruction of red corpuscles is furnished by the presence in the blood, in various situations of the body, of a pigment containing iron and the presence of pigments in the bile and urine, all of which are believed to be derivatives of effete hemoglobin. The blood-pigment (hematin), which contains the iron of the hemoglobin, is found in the capillaries of the liver, in the cells of the splenic pulp, and in the marrow of the bones. Whether the presence of the pigment in these organs is a proof that the corpuscles are destroyed here, or whether they are to be regarded merely as agents concerned in the further reduction and elimination of the hematin, is uncertain. The genetic relationship between bile-pigment and hemoglobin is shown by the fact that any artificial destruction of hemoglobin or its injection into the blood is attended by an increase in the quantity of bile-pigment eliminated. It appears also from chemic considerations that the hemoglobin will undergo cleavage into a globulin body and hematin, which by the loss of its iron is readily converted into the bile-pigment, bilirubin. The amount of this latter pigment may therefore be taken as an index of the extent of corpuscular destruction.

There is some evidence for the view that the iron set free by the reduction of the hematin, eventually reaches the blood-making organs and is utilized by the developing corpuscles in the formation of the necessary hemoglobin.

This gradual decay of corpuscles as well as the losses occasioned by hemorrhages necessitate a continuous formation of new corpuscles, so that the normal number may be maintained. The rapidity with which corpuscles may be renewed, in the woman at least, is shown by a computation of Mr. Charles L. Mix. A woman loses during a menstrual period 150 c.c. of blood. At the end of twenty-eight or thirty days this volume is restored, so that in one day 5 c.c., or 5000 c.mm., of blood must be formed, or 208 c.mm. per hour and 3½ c.mm. per minute. That is, during a certain number of years 15,750,000 corpuscles must be formed every minute, and this independent of the daily loss due to functional activity.

At the present time there is a general agreement among histologists that in adult life the red corpuscles are derived from embryonic forms, the so-called erythroblasts, cells of a large size with distinctly reticulated nuclei, which are found chiefly in the red marrow of the long bones.[1] In this situation both arterial and venous capillaries are relatively large and the blood is separated from the surrounding marrow by extremely thin walls. In the passages of this capillary network the erythroblasts make their appearance most probably by a transformation of pre-existing marrow cells which cross the capillary wall from without. At first they are large, homogeneous, colorless, perhaps slightly tinged with hemoglobin and distinctly nucleated. They increase in number by karyokinesis and at the same time increase in their hemoglobin content. In the course of their development the nucleus becomes smaller and denser, when the cells are known as normoblasts. Subsequently the nucleus is extruded, carrying with it a portion of the perinuclear cytoplasm, after which the remainder of the corpuscle assumes the shape and size of the adult corpuscle and is carried out into the general circulation. After severe hemorrhage the formative processes in the marrow may become so active that erythroblasts and normoblasts make their appearance in the blood-stream before the extrusion of the nucleus has taken place.

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[1] For an admirable résumé of the various views regarding the origin and formation of red corpuscles see the paper of Mr. Charles L. Mix, Boston Med. and Surg. Journal, 1892, Nos. 11 and 12; also paper by Prof. W. H. Howell, Journal of Morphology, vol. iv, 1892.

The Corpuscles of Other Vertebrated Animals.—In all mammals, with the exception of the camel, llama, and dromedary, the red corpuscles present the same shape and structure as the corpuscles of man, and may be described as circular, flattened, biconcave discs. In the animals excepted the corpuscles are oval. The size, however, varies in different animals from 0.0092 mm. ($\frac{1}{2745}$ inch) in the elephant to 0.0023 mm. ($\frac{1}{12325}$ inch) in the musk-deer, while in most animals the average lies between 0.0084 mm. and 0.0050 mm. Inasmuch as the question may arise as to whether the corpuscles of any given specimen of blood are those of a human being or of some other mammal, a knowledge of the size of the corpuscles is a matter of medicolegal as well as of physiologic interest. Though the differences in size are slight, yet it is possible for skilled microscopists, when examining fresh blood, to make a diagnosis between the corpuscles of man and those of the domesticated animals, with the exception, perhaps, of the guinea-pig. The diagnosis of the corpuscles of dried blood which have been altered by the action of various external agents, even though capable of a certain degree of restoration, is most difficult, and should not be attempted in criminal cases without large experience in microscopy, in measurements and methods of preparation of all kinds of blood-corpuscles, and a proper conception of corpuscular forms and sizes. In the following table the average results of the measurements of the corpuscles in different classes of animals are given (abstracted from Formad's compilation):

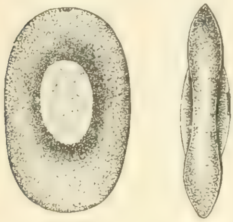


FIG. 106. FIG. 107.
AMPHIBIAN COLORED BLOOD-CORPUSCLES. Fig. 106, on the flat; Fig. 107, on edge. — (*Landois and Stirling.*)

	Gulliver		Wormley		C. Schmidt Mallinin		French Medicolegal Soc. Welcker		Formad	
	Inch	Mm.	Inch	Mm.	Inch	Mm.	Inch	Mm.	Inch	Mm.
Man	1.3200	0.0079	1.3250	0.0078	1.3300	0.0077	1.3257	0.0078	1.3200	0.0079
Guinea-pig	1.3538	0.0071	1.3223	0.0079	1.3300*	0.0077	1.3213†	0.0079	1.3400	0.0075
Dog	1.3532	0.0071	1.3561	0.0071	1.3636	0.0070	1.3485	0.0073	1.3580	0.0071
Rabbit	1.3607	0.0070	1.3653	0.0070	1.3968	0.0064	1.3653	0.0069	1.3662	0.0069
Ox	1.4267	0.0060	1.4219	0.0060	1.4354	0.0058	1.4545	0.0056	1.4200	0.0060
Pig	1.4230	0.0060	1.4268	0.0059	1.4098	0.0062	1.4098	0.0062	1.4250	0.0060
Horse	1.4600	0.0057	1.4243	0.0059	1.4464	0.0057	1.4545	0.0056	1.4310	0.0059
Cat	1.4400	0.0058	1.4372	0.0058	1.4545	0.0056	1.3922	0.0065	......	......
Sheep	1.5300	0.0048	1.4912	0.0031	1.5649	0.0045	1.5076	0.0059	1.5000	0.0051
Goat	1.6366	0.0040	1.6189	0.0041	1.6369	0.0040	1.5525	0.0046	1.6100	0.0042

* Masson. † Woodward.

In birds, reptiles, and amphibians the corpuscles are larger than in mammals, are oval in shape, and nucleated. (See Figs. 106 and 107.) As the scale of animal life is descended the corpuscles increase in size, until in Proteus and Amphiuma the long diameter attains an average length of 0.058 mm. and 0.077 mm. respectively. In fish the corpuscles are smaller, oval, and nucleated, with the exception of the lamprey eels, in which they are circular, biconcave, and nucleated, though the nucleus is generally concealed in the peripheral portion of the corpuscle. As in these animals the corpuscles are almost twice the size of the human red corpuscles, they can, notwithstanding the similarity of shape, be readily distinguished from them.

The Function of the Red Corpuscles.—The red corpuscles, by virtue of the capacity of their contained hemoglobin for oxygen absorption, may be regarded as carriers of oxygen from the lungs to the tissues, and therefore important factors in the general respiratory process. The size as well as the number of the corpuscles in different classes of animals appears to be directly related to the activity of the respiratory process. In those animals in which the corpuscles are small and numerous and the total superficial area large, respiration is active, the quantity of oxygen absorbed is large, and the energy liberated through oxidation is correspondingly large. In those animals, on the contrary, in which the corpuscles are large and relatively few in number, the reverse conditions obtain. This is in accordance with the fact that the superficial area of any given volume of substance is increased in proportion to the extent to which it is subdivided.

The superficial area of a single human red corpuscle has been estimated at 0.000128 sq. mm. If the number of corpuscles in 1 cubic millimeter of blood averages 5,000,000, the superficial area would amount to 640 square millimeters; and if the amount of blood in the body of a man weighing 70 kilos is taken as one-nineteenth of this weight—that is, 3864 grams (3659 c.c.) —the total area of the corpuscular surface will amount to 2341 square meters.

HISTOLOGY OF THE WHITE CORPUSCLES OR LEUKOCYTES

The presence of white corpuscles in the blood can be readily observed under the same conditions as the red corpuscles are observed. Thus when the mesentery of the frog or the guinea-pig is examined with the microscope the white corpuscles are seen adhering to the walls of the blood-vessels; in a drop of freshly drawn blood they are found in the spaces between red corpuscles (Fig. 93). A careful examination of the blood by the employment of appropriate methods has revealed the presence of several varieties of white corpuscles, to which reference will be made in a subsequent paragraph.

Shape and Size.—In the resting condition, whether seen in the vessel or on the stage of the microscope, the white corpuscle, as its name implies, is grayish in color, round or globular in form, though often presenting a more or less irregular surface. Its diameter varies from 0.004 to 0.013 mm., though the average is about 0.011 mm. or about $\frac{1}{2500}$ inch.

Structure.—A typical white corpuscle consists of a ground-substance uniformly transparent and apparently homogeneous, in which are embedded a number of granules of varying size, some of which are very fine, while others are large. By various reagents it has been demonstrated that the granules are fatty, protein, and carbohydrate (glycogen) in character. In the fresh cells the existence of a nucleus is difficult of detection, though its presence can be demonstrated by the addition of acetic acid, which renders the perinuclear cytoplasm more transparent and makes the nucleus conspicuous and sharply defined. From its structure it is apparent that the white corpuscle belongs to the group of undifferentiated tissues and resembles the cells of the embryo in its earliest stages as well as the unicellular organism, the amœba.

Chemic Composition.—The chemic composition of the white corpuscles has been inferred from an analysis of pus-corpuscles, with which they are practically identical, and of lymph-corpuscles from the lymph-glands. Of the corpuscle about 90 per cent. is water and the remainder solid matter consisting mainly of proteins, of which nuclein, nucleo-albumin, and cell globulin are the most abundant. The two former are characterized by the presence of a considerable quantity of phosphorus, amounting to as much as 10 per cent. Lecithin, fat, glycogen, and earthy and alkaline phosphates are also present.

Number of White Corpuscles.—The number of white corpuscles per cubic millimeter of blood is much less than the number of red corpuscles, the ratio being in the neighborhood of 1 white to 700 red. This ratio, however, varies within wide limits in different portions of the body and under normal variations in physiologic conditions. In the blood of the splenic artery there is but 1 white to 2260 red, while in the splenic vein there is 1 white to every 60 red; or about thirty-eight times as many as in the artery. In the portal vein there is 1 white to 740 red, while in the hepatic vein there is 1 white to 170 red.

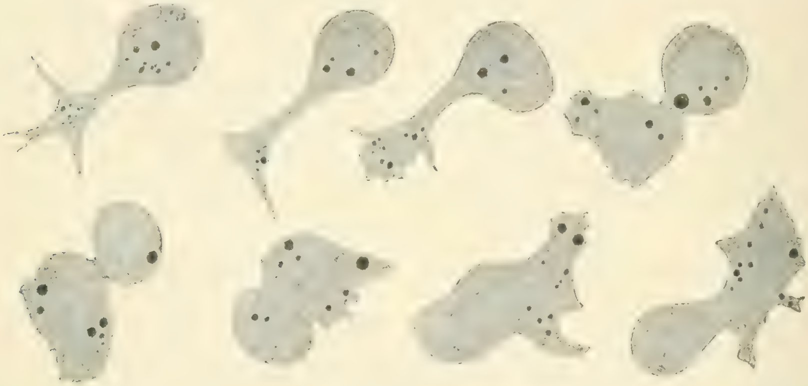


FIG. 108.—AMŒBOID MOVEMENTS OF A WHITE CORPUSCLE FROM THE FROG. The form changes occurred within ten minutes. The black particles are Chinese ink which had been injected twenty-four hours before into the dorsal lymph sac.—(*Rauber-Kopsch.*)

The total number of white corpuscles per cubic millimeter has been estimated at from 5000 to 10,000, though the average is about 7500. The number, however, is influenced by a variety of physiologic conditions. The ingestion of food rich in protein material raises the count from 30 to 40 per cent., as compared with the count before the meal. In the new-born the number is greater than in adults—17,000 to 20,000 per cubic millimeter. Cabot states that 30,000 is never a high count after a meal in infants under two years. In the later months of pregnancy, especially in primiparæ, the number increases to 16,000 to 18,000. Many pathologic conditions of the body also influence the count very considerably.

Fasting for a few days always lowers the count, and in a case of total abstinence of food for a week, reported by Luciani, the count fell to 861 per cubic millimeter, after which it rose to 1530, where it practically remained for the succeeding three weeks of the fasting period.

When the number of leukocytes present in the peripheral blood exceeds the normal, *i.e.*, 10,000 per cubic millimeter the condition is termed *leukocytosis;* when the number falls below the normal the condition is termed *leukopenia.* Both conditions, however, may be only temporary and therefore physiologic, or they may be permanent, associated with certain diseased states of the body and therefore pathologic. It is therefore permissible to speak of a physiologic and a pathologic leukocytosis and leukopenia.

The method for counting the white corpuscles is similar to that used in counting the red corpuscles. The given volume of blood should, however, be diluted with 10 or 20 volumes of a one per cent. solution of acetic acid, which disintegrates the red corpuscles and thus facilitates the counting of the white. The pipette should have a larger bore than that used for the red, and a much greater number of squares in the counting chamber should be counted, so as to diminish the percentage of error.

Physiologic Properties.—The white corpuscles and especially the leukocytes possess the characteristic property of exhibiting movements similar to those exhibited by the amœba, and are therefore termed amœboid. These movements consist in alternate protrusions and retractions of portions of the cell body, as a result of which they present from moment to moment, a great variety of forms. (See Fig. 108.) The protruded process, the pseudopod, can also attach itself to some point of the surface on which it rests, and then draw the body of the corpuscle after it. By a repetition of this process the corpuscle can slowly creep about and change its position in reference to its environment. By virtue of these amœboid movements the corpuscle can appropriate small particles of pigment, such as indigo or carmine, and after a short time eliminate them from various parts of the surface. It is also capable of thrusting a process into and through the wall of the capillary vessel, after which the remainder of the corpuscle follows (Fig. 109). This continues until the corpuscle is outside the vessel and in the lymph-space, where it resumes its original shape and movement. This process is best observed in inflammatory conditions, when the blood has come to rest and the vessels are occluded with both red and white corpuscles. To this passage of the white blood-corpuscles through the capillary wall the term *diapedesis* is given. The movements of the white corpuscles are increased by a rise in temperature up to 40°C., beyond which they cease, owing to the coagulation of the cell-substance. A low temperature also arrests the movements. Induced electric currents also cause contraction and death of the cell. Moisture and oxygen are necessary to their activity.

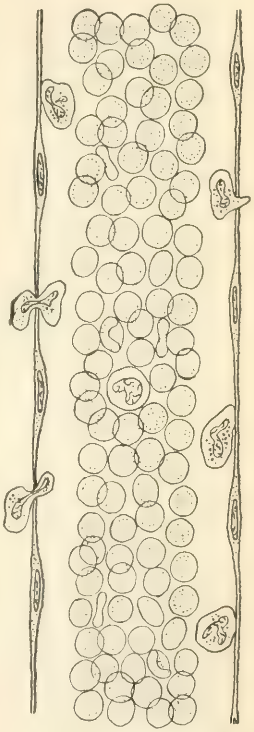


FIG. 109.—SMALL VESSEL SHOWING VARIOUS STAGES IN THE DIAPEDESIS OF LEUKOCYTES.—(*G. Bachman.*)

From their similarity to lower organisms the white corpuscles may be regarded as independent organisms living in the animal fluids, just as the amœba lives in its natural liquid medium.

Varieties of Leukocytes.—A detailed study of the blood with the aid of the triacid staining fluid of Ehrlich or any of the various eosin and methylene-blue stains, reveals the presence of five distinct varieties of leukocytes and transitional forms which may be classified as follows:

1. *Small lymphocytes*, so called from their resemblance to the corpuscles of the lymph-glands, consisting of a deeply staining and relatively large round nucleus, encircled by a narrow rim of cytoplasm. Found in from 20 to 25 per cent. of all leukocytes. They vary in size from 0.004 to 0.007 mm.
2. *Large lymphocytes* or hyaline cells, which are believed by some to represent the preceding type at a later stage of development, by others to have an independent origin, are distinguished by a round or ovoid nucleus staining faintly and surrounded by a relatively larger layer of cytoplasm than is seen in the small lymphocyte. The large lymphocyte is present to the extent of from 4 to 8 per cent. Transitional forms, usually present from 1 to 2 per cent. are very much like the large lymphocyte in appearance and size, with the exception, however, that they possess a cresentic or indented nucleus and have a somewhat greater affinity for basic dyes. They are usually counted with the large lymphocytes.

   Both varieties of lymphocytes are characterized by a cytoplasm which is devoid of granules. Rarely, basophilic granules may be present.
3. *Polymorphonuclear neutrophiles.* The nucleus of this cell is irregular and assumes a great variety of shapes in different cells, a feature which has suggested the name given to the cell. The perinuclear cystoplasm contains a large number of fine granules which are neutrophilic or faintly acidophilic in their staining reaction. They make up about 60 to 70 per cent. of the whole number of the white blood-cells. They vary in size from 0.007 to 0.010 of a mm.
4. *Eosinophile cells.* The nucleus resembles in many respects that of the preceding variety; it is, however, less apt to stain so deeply. It is also very irregular in shape and many cells possess several apparently distinct nuclei. The cytoplasm is ill-defined but its presence is easily revealed through the large, intensely acidophilic granules which it possesses.

   It is present to the extent of 0.5 to 2 per cent.
5. *Basophile cells*, the nucleus of which is round or slightly irregular. The granules, which may be large or small, are basophilic and stain more deeply than the nucleus, though they have the same color. It is rare for this cell to be present above 0.5 per cent. of all leukocytes.

   In abnormal states of the blood other forms of leukocytes are frequently present, *e.g.*, myelocytes, leukoblasts, myeloplaxes, etc., the significance of which is not always apparent.

Origin of the White Corpuscles.—Of the various theories advanced to explain the origin of leukocytes, that formulated by Ehrlich has found the most credence. According to this theory the leukocytes may genetically be classed into two groups. In the first group are the large and small lympho-

(*Triacid Stain.*)

1, 2, 3, 4. **Small Lymphocytes.**
Contrast the faintly colored protoplasm of these cells in the triple stained specimen, with their intensely basic protoplasm in the film stained with eosin and methylene-blue, 17 and 18. The cell body of 1 is invisible. Note the kidney-shaped nucleus in 4.

5, 6. **Large Lymphocytes.**
With this stain the nucleus reacts more strongly than the protoplasm; with eosin and methylene-blue (19, 20), on the contrary, the protoplasm is so deeply stained that the nucleus appears pale by contrast. This peculiarity is also observed in the smaller forms of lymphocytes.

7, 8. **Transitional Forms.**
Note the moderately basic and indented nucleus, and the almost hyaline non-granular protoplasm. Compare 8 with the myelocyte, 7, Plate I, these cells differing chiefly in that the myelocyte contains neutrophile granules.

9, 10, 11. **Polynuclear Neutrophiles.**
These cells are characterized by a polymorphous or polynuclear nucleus, surrounded by a cell-body filled with fine neutrophile granules. In 11 the nuclear structure is obviously separated into four parts; in 9 it is moderately, and in 10 markedly, polymorphous.

12, 13. **Eosinophiles.**
The nuclei are not unlike those of the polynuclear neutrophile, except that they are somewhat less convoluted, and poorer in chromatin, staining less intensely. The protoplasm is filled with coarse eosinophile granules, the characteristics of which are clearly illustrated by 13, a "fractured" eosinophile.

14. **Eosinophile Myelocyte.**
Compare with 15.

15, 16. **Myelocytes.** (*Neutrophilic.*)
These cells are morphologically similar to 14, except that they contain neutrophile instead of eosinophile granules. Note that the granules of the myelocyte are identical with those of the polynuclear neutrophile. A dwarf form of myelocyte is represented by 16.

(*Eosin and Methylene-blue.*)

17, 18. **Small Lymphocytes.**
Note the narrow rim of pseudo-granular basic protoplasm surrounding the nucleus, and the pale appearance of the latter.

19, 20. **Large Lymphocytes.**
Budding of the basic zone of protoplasm is represented by 20. Both of these cells belong to the same type as 5 and 6.

21, 22. **Large Mononuclear Leukocytes.**
Compared with 19 and 20, these cells have a decidedly less basic protoplasm, but a somewhat more basic nucleus. In the triple stained film these differences cannot be detected, so that they must be classed as large lymphocytes.

23. **Transitional Form.**
The distinction between this cell and 24 is not marked; the nucleus of the latter simply being somewhat more basic and convoluted.

24, 25, 26, 27. **Polynuclear Neutrophiles.**
With this stain these cells show a feebly acid protoplasm, and lack granules. Note that the more twisted the nucleus the deeper it is stained. Compare with 9, 10 and 11.

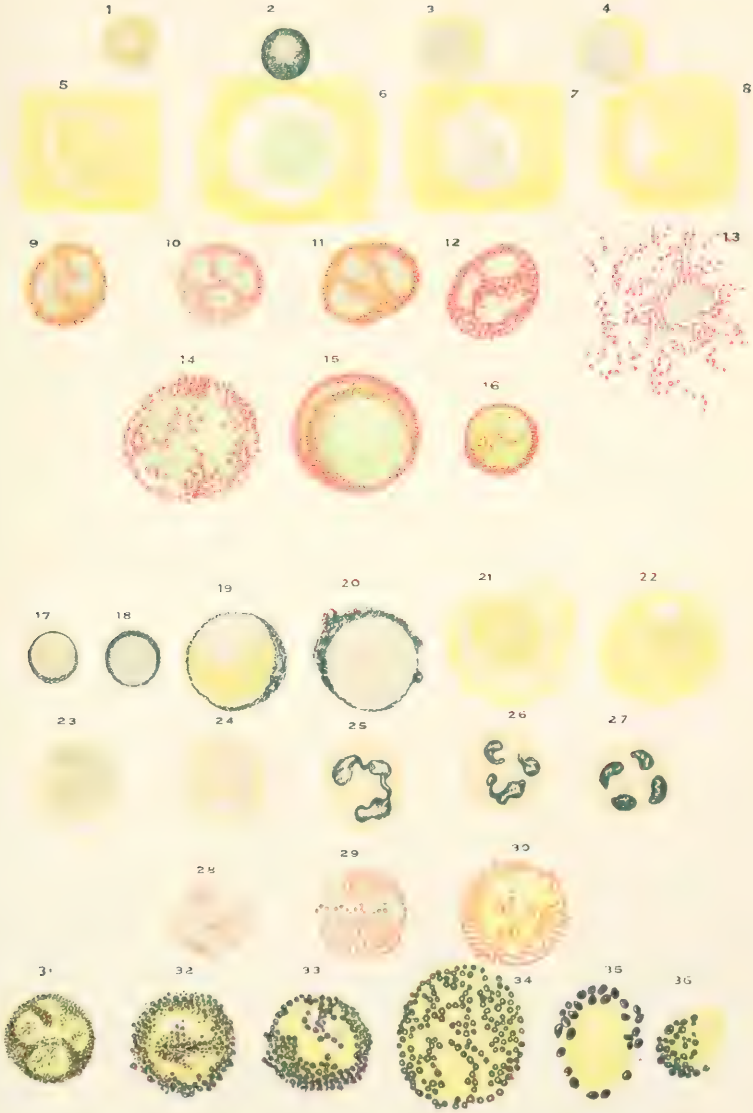
28, 29. **Eosinophiles.**
Compare with 12 and 13.

30. **Eosinophilic Myelocyte.**
Compare with 14.

31. **Basophile.** (*Finely granular.*)
This cell is characterized by the presence of exceedingly fine δ-granules, staining the *pure* color of the basic dye. The nucleus is markedly convoluted and deficient in chromatin. The cell here shown was found in normal blood.

32, 33, 34, 35, 36. **Mast Cells.**
The granules take a *modified* basic color, as shown by their royal-purple tint in this illustration. Note their unusually large size and ovoid shape in 35, their peculiar distribution in 35 and 36, and their irregularity in size in 32 and 36. With the triacid mixture these granules, as well as those of the finely granular basophile, 31, remain unstained, showing as dull-white stippled areas in the cell-body. The nuclear chromatin of the mast cell is so delicate and so feebly stained that it is barely visible. These cells were found in the blood of a case of splenomedullary leukemia.

PLATE I.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THE LEUKOCYTES.

(2-16, *Triacid Stain;* 17-36, *Eosin and Methylene-blue.*)

(E. F. FABER, *fec.*)

(*From DaCosta's "Clinical Hematology."*)

cytes which take their origin entirely from the lymph-adenoid tissues of the body, *e.g.*, the lymph-glands, solitary and agminated follicles of the intestines, etc. As the lymph flows through these structures the lymph-corpuscles, as the future lymphocytes of the blood are called in these situations, are washed out and carried by way of the lymph-stream into the general circulation.

In the second group are the transitional forms, the polymorphonuclear, eosinophile and basophile leukocytes which originate from the bone-marrow only. The immediate ancestors of these cells are known as myelocytes and are normally found in the red bone-marrow. These cells, through transitional stages, assume the characteristics of the leukocytes just mentioned and pass directly into the capillaries of the marrow whence they are distributed throughout the body.

Several attempts have been made by different investigators to trace all varieties of leukocytes to a common mother cell. While this is believed to take place during embryonal life, the proofs of such an origin of leukocytes in the normal adult are insufficient and unconvincing.

After an unknown period of life the leukocytes undergo dissolution and disappear.

Functions.—The functions of the white corpuscles are but imperfectly known, and at present no positive statements can be made. It has been suggested that wherever found in the body, whether in blood or tissues, they are engaged in the removal of more or less insoluble particles of disintegrated tissues, in attacking and destroying more or less effectively various forms of invading bacteria and thus protecting the body against their deleterious activity. This they do by surrounding, enveloping, and incorporating either the tissue particle or bacterium and digesting it. On account of this swallowing action these cells were termed by Metchnikoff *phagocytes* and the process *phagocytosis*. In their capacity as phagocytes it has been assumed that they are made more or less efficient by the presence in the plasma of an agent or agents which in some unknown manner render the bacteria less resisting and thus make them more susceptible to the attacks of the leukocytes. These agents which are supposed to be secreted by the tissue cells are termed *opsonins*, from their supposed function, that of preparing the bacteria for leukocytic digestion. The cells engaged in this process are the polymorphonuclear leukocytes and the large and the small lymphocytes. He regards them as the general scavengers of the body. It has been suggested that they are also engaged in the absorption of fat from the lymphoid tissue of the intestine. In their dissolution they contribute to the blood-plasma certain protein materials which assist under favorable circumstances in the coagulation of the blood.

HISTOLOGY OF THE BLOOD-PLATELETS

The blood-platelets or plaques are small histologic elements circulating in the blood-plasma. They were discovered and described in 1845 by Arnold. Hayem, later applied to them the term hematoblasts, on the supposition that they were the early stages in the development of the red corpuscles. This is now known to be erroneous. On account of their specific, distinct characters, and their constant presence in the blood of living animals (guinea-pig and bat), they are now regarded as normal constituents of the blood and designated sometimes as the third corpuscle. When blood is freshly drawn from the body, the plaques rapidly undergo disintegration and disappear; but by treating the blood with osmic acid, the form and structure of the plaque may be retained. They may also be preserved by preparing and staining the tissues with Wright's blood stain.

The blood-platelet may be defined as a colorless, grayish-white, homogeneous or finely granular protoplasmic disc, varying in diameter from 1.5 to 3.5 micro-millimeters. The edges are rounded and well defined, but it is not certain whether they are only flattened or are slightly biconcave. There is, however, no nucleus, though the central portion is granular and the peripheral portion clear. The ratio of the plaques to the red corpuscles is 1 to 18 or 20, and the total number per cubic millimeter has been estimated to be 250,000 to 300,000 or more.

When blood is shed they tend to adhere to each other and form irregular masses known as Schultze's granular masses. If threads are suspended in blood, the plaques accumulate in enormous numbers upon them and appear to form a center from which fibrin filaments radiate as coagulation proceeds. The white thrombi which form in blood-vessels in consequence of diseased states—*e.g.*, endocarditis, atheromatous ulceration, etc.—are composed very largely of blood-plaques and fibrin threads.

The blood-plaques can be seen with high powers of the microscope in the blood-vessels of the omentum of the guinea-pig and rat, especially when the blood-stream begins to slow. They are also readily seen in the blood-vessels of subcutaneous connective tissue of various animals, and especially in that of the new-born rat. A small quantity of this tissue moistened with normal saline and examined microscopically with suitable powers will show large numbers of plaques within the blood-vessels.

As to the origin of the blood-platelets there has been much difference of opinion. Many theories have been proposed, none of which have been accepted. As a result of long-continued observations Wright has recently published results which make it probable that they are fragments or detached portions of the cytoplasm of giant cells, megakaryocytes, found in the marrow of the bones. The cytoplasm is prolonged into pseudopod-like processes which become detached, and as they are in close relation to the blood channels they are soon taken up and carried into the blood of the general circulation when they are known as blood-platelets or plaques.

The function of the blood-plaques is unknown, but it has been surmised that in some way they are, like the leukocytes, concerned in the coagulation of the blood. Whenever they are diminished in number, as in purpura and hemophilia, coagulation takes place very slowly.

THE TOTAL QUANTITY OF THE BLOOD; ITS GENERAL COMPOSITION

The determination of the total quantity of the blood in an animal is best made by the chromometric method, somewhat modified at present, of Welcker. This consists, first, in bleeding an animal, collecting all the blood it yields, and weighing it; second, in washing out the vessels with a normal saline solution until the fluid comes from the veins clear and free from blood; third, in mincing the tissues of the body, after removal of the contents of the alimentary canal, soaking them in water for twenty-four hours, and then expressing them. All the washings are collected and weighed. A given volume of the normal defibrinated blood, treated with carbon monoxid so as to give it uniform color, is then diluted with water until its tint is identical with that of the washings similarly treated with carbon monoxid. From the quantity of water necessary to dilute the blood the quantity of blood in the washings is readily determined. The animal having been previously weighed and the weight of the contents of the alimentary canal deducted, the ratio of the total weight of the blood to the weight of the body at once becomes apparent. By this method it has been shown that the ratio of blood to body-weight in a human adult is 1 : 13; in an infant, 1 : 19; in a dog, 1 : 13; in a cat, 1 : 21.

The more recent investigations of Haldane and Smith and of Plesch with the employment of a different method make it probable that the ratio is approximately 1 : 19. Thus a man weighing 70 kilos would have 3684 grams of blood.

The amount of blood in the different organs has been determined by ligating the blood-vessels in the living animal, removing the organ, and after allowing the blood to escape subjecting the tissues to the chromometric methods described above. According to Ranke, the volume of the blood is distributed as follows: Heart, lungs, arteries, and veins, ¼; liver, ¼; muscles, ¼; other organs, ¼.

General Composition.—The results of the analyses of the blood will vary with the animal and the methods employed. The following table, taken from Gad, shows the average composition, expressed in whole numbers, of horse's blood. In essential respects the ratio of the constituents in human blood would not be materially different.

One thousand parts of blood contain:

Cells	328	Water	200		200
		Solids	128	Hemoglobin	116
				Other organic matter	10
				Salts	2
Plasma	672	Water	604		604
		Solids	68	Fibrin	7
				Albumin	52
				Fat	1
				Other organic matter	3
				Potassium and sodium salts	4
				Calcium and magnesium salts	1

CHEMISTRY OF COAGULATION

The changes which eventuate in the formation of fibrin, and hence all the subsequent phenomena of coagulation, are chemic in character; but as these changes take place in organic compounds the composition of which is but imperfectly known, the intimate nature of the process is quite obscure. All the theories which have been advanced in explanation, though approximating the truth, are more or less incomplete and in some respects contradictory. Since the coagulation is coincident with the appearance of the fibrin, the antecedents of this substance, the physical and chemic conditions which condition its development, and the succession of chemic changes involved must be determined, before any consistent theory can be established.

Extra-vascular Coagulation.—At present it is generally believed that the immediate factors concerned in extra-vascular coagulation are fibrinogen, a calcium salt, and an agent thrombin. As to the manner in which these three bodies react one with another there is a diversity of opinion.

As an outcome of a long series of experiments that have been performed to determine the nature and the succession of the chemic phenomena underlying the coagulation of the blood, the following facts seem to be well established, viz: the immediate cause of the coagulation is the appearance of *fibrin*, a derivative of an antecedent substance always present in the blood termed *fibrinogen;* the cause of the conversion of the soluble fibrinogen into the insoluble fibrin is the presence and activity, under the circumstances, of an agent termed *thrombin*, the chemic nature of which is a subject of discussion. By some chemists it is regarded as a ferment which causes a molecular rearrangement of the fibrinogen; by others it is regarded as a definite organic colloidal body which unites in some physico-chemic manner with the fibrinogen to form fibrin.

The crux of the problem is the source and the conditions necessary for the production of the thrombin. It is generally conceded that thrombin is a derivative of an antecedent substance *prothrombin* or *thrombogen*, a substance always present in the blood plasma, a product of the decomposition of blood-platelets and leukocytes. With prothrombin there is physiologically associated a calcium salt, the presence of which is absolutely essential for coagulation or the conversion of prothrombin into thrombin as was conclusively shown by Arthus and Pages: For if it is precipitated by the addition of oxalate of potassium, coagulation will not take place. At all times then, there are present in the blood, prothrombin, a calcium salt and fibrinogen. Given the two former factors, the question arises, why do they not react to form thrombin in the circulating blood, and why do they so react in shed blood?

The answer of Morawitz is, that prothrombin requires an activating agent, a *kinase* which is wanting in circulating blood but is present in shed blood. It is supposed to develop in the disintegration of the cell elements of the blood, leukocytes and blood-platelets, and perhaps from the cell elements of the injured tissues as the blood flows over them. Shortly after its appearance the kinase, with the aid of the calcium salt converts the prothrombin into thrombin, after which it unites with fibrinogen to form fibrin. For this reason the kinase has been termed *thrombo-kinase.*

The answer of Howell to the foregoing question is somewhat different and based on a long series of experiments recently published. From the results of these experiments the answer given is that prothrombin is prevented from reacting with the calcium salt to form thrombin in the circulating blood, by reason of the presence and possible union with prothrombin of an agent termed *anti-thrombin.* So long as this relation is not disturbed the blood remains fluid. When blood is shed there is supposed to develop from the cell elements of the blood, the leukocytes and blood-platelets, and perhaps from the cell elements of the injured tissues as well, a *plastin*, the specific action of which is to combine with the anti-thrombin and thus set free the prothrombin. This having been accomplished the calcium salt activates the prothrombin, and converts it into thrombin, after which it combines with the fibrinogen. For this reason the plastic agent has been termed *thrombo-plastin.* Experiments indicate that this agent belongs to the group of bodies known as phosphatids and similar in its properties to one member of this group, viz., *kephalin.*

Intra-vascular Coagulation.—So long as the relations of the blood and the vascular apparatus remain physiologic, no coagulation occurs in the vessels. The reasons assigned for this are: (1) the absence of thrombo-kinase in sufficient amounts; or (2) the presence of anti-thrombin. On either assumption the reaction between prothrombin and calcium with the formation of thrombin does not take place. If the vessels are injured as they are when ligated or torn or in any way impaired, coagulation promptly takes place with the subsequent occlusion of the vessel. As to whether the injured tissues or the blood-cells now generate an agent, thrombo-kinase, which activates the prothrombin and calcium, or whether they generate an agent thrombo-plastin, which neutralizes an anti-thrombin, is a subject of discussion.

Under pathologic conditions of the circulatory apparatus, especially of the internal lining, intra-vascular coagulation frequently arises, though the process cannot be considered as identical with extra-vascular coagulation. Many pathologists assert that in its origin, mode of formation, and structure the intra-vascular coagulum or thrombus is not a true coagulum as ordinarily understood, but rather a conglutination of blood-plaques and leukocytes. Whenever the integrity of the internal wall of the vessel is impaired by disease or by the introduction of foreign bodies, there is primarily a deposition and accumulation of blood-plaques at the injured area or on the foreign body which constitutes to a large extent the mass of the thrombus which at once forms. The thrombi which form on the surface of atheromatous ulcers, on the valves of the heart, and in the veins in consequence of diseased states, on threads or needles passed through the vessels, at the orifices of torn blood-vessels, consist largely of blood-plaques. A thrombus so formed may contain a number of delicate fibrin threads, which, however, present a different appearance from the fibrin of the extra-vascular clot. In the thrombi which form around foreign bodies there is a larger quantity of fibrin than in those originating from causes wholly within the vessel.

CHAPTER XIII

THE CIRCULATION OF THE BLOOD

Each organ and tissue of the body is the seat of a more or less active metabolism, the maintenance of which is essential to its physiologic activity. This metabolism is characterized by the assimilation of food materials and the production of waste products; that it may be maintained it is imperative that there shall be a continuous supply of the former and a continuous removal of the latter. Both conditions are subserved by the blood. In order, however, that this fluid may fulfil these functions it must be kept in continuous movement, must flow into and out of the tissues in volumes varying with their activity, with a certain velocity and under a given pressure.

The apparatus by which these results are attained is termed **the circulatory apparatus.** This consists of a central organ, the heart; a series of branching diverging tubes, the arteries; a network of minute passageways with extremely delicate walls, the capillaries; a series of converging tubes, the veins. These structures are so arranged as to form a closed system of vessels within which the blood is kept in continuous movement mainly by the pressure produced by the pumping action of the heart, though aided by other forces. (See Fig. 110.)

In this system a particle of blood which passes any given point will eventually return to the same point, no matter how intricate or tortuous the route may be through which it in the meanwhile travels; for this reason the blood is said to move in a circle, and the movement itself is termed the circulation.

In order to understand the reasons for the movement of the blood in one direction only, as well as for many other phenomena connected with the circulation, a knowledge of the structure of the heart and its internal mechanism is of primary importance.

THE PHYSIOLOGIC ANATOMY OF THE HEART

The heart is a conic or pyramid-shaped hollow muscle situated in the thorax just behind the sternum. The base is directed upward and to the right side; the apex downward and to the left side, extending as far as the space between the cartilages of the fifth and sixth ribs. In this situation the heart is enclosed and suspended in a fibro-serous sac, the *pericardium*, attached to the great vessels at its base.

The heart is a hollow, double muscle organ, consisting of a *right* and a *left* half, separated by a musculo-membranous septum. The general cavity of each side is subdivided by an incomplete transverse fibrous septum into two smaller cavities, an upper and a lower, known respectively as the *auricle* and the *ventricle*. The heart may therefore be said to consist of four cavities, the walls of which are composed of muscle-tissue. Of these four cavities, the right auricle and the right ventricle constitute *venous* the heart; the left auricle and the left ventricle, the *arterial* heart.

The right auricle is quadrangular in shape and presents on its posterior aspect two large openings, the terminations of the two final trunks of the venous system, the *superior* and *inferior vena cava* (Fig. 111). Below the auricle communicates with the ventricle by a large opening which, from its position, is termed the *auriculo-ventricular* opening. The walls of the auricle are extremely thin, not measuring more than two millimeters in thickness.

The right ventricle, as shown on cross-section, is crescentic in shape owing to the projection of the ventricular septum. It presents at its upper left angle a cone-shaped prolongation, the *conus arteriosus*. From this prolongation, and continuous with it, arises the pulmonic artery. The wall of the ventricle measures in the middle about four millimeters in thickness. The inner surfaces of the ventricle show: (1) a complicated system of muscle ridges and bands, the *columnæ carneæ* (fleshy columns), and (2) a set of muscle projections, the *musculi papillares* (papillary muscles), which arise by a broad base from the walls of the ventricle and project upward toward the auriculo-ventricular opening. From the apex of each papillary muscle there are given off fine tendinous cords, the *chordæ tendineæ*, which become attached above to the under surface of the auriculo-ventricular valve.

The left auricle, similar in general shape to the right, presents posteriorly four openings, the terminations of the four final trunks of the venous system of the lungs, the pulmonary veins. Below is found the corresponding auriculo-ventricular opening. The wall of the auricle measures about 3 mm. in thickness. The left ventricle (Fig. 112) is conic in shape from above downward and oval or circular in shape on cross-section. At its upper inner angle it presents a circular orifice, the margins of which give attachment to the walls of the aorta, the main arterial trunk of the systemic circulation. The inner surfaces of the ventricle show a similar though better-developed system of columnæ carneæ, musculi papillares, chordæ tendineæ, etc. The wall of the left ventricle measures about 11.5 mm. in thickness in the middle.

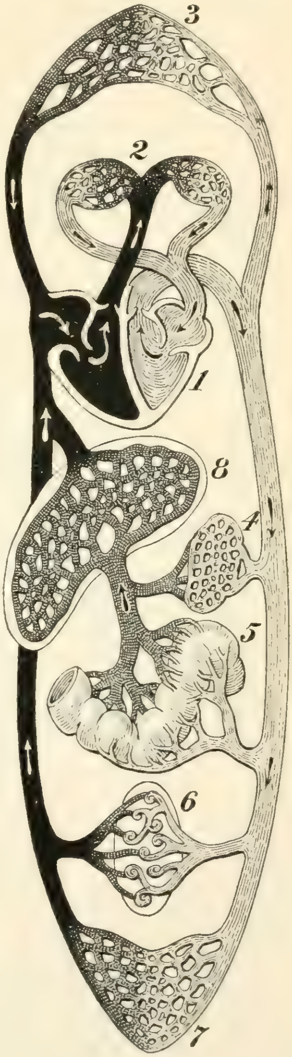

FIG. 110.—DIAGRAM OF THE CIRCULATION. 1. Heart. 2. Lungs. 3. Head and upper extremities. 4. Spleen. 5. Intestines. 6. Kidney. 7. Lower extremities. 8. Liver.—(*After Dalton.*)

The Endocardium.—The cavities of both the right and left sides of the heart are lined by a thin, firm connective-tissue membrane, closely adherent to the muscle-tissue, termed the endocardium. It contains also elastic fibers and smooth muscle-fibers. Its entire surface is covered with a layer of polygonal endothelial cells. This membrane serves partially to resist undue distention of the heart during contraction and to prevent separation of the muscle-fibers. The endocardium is continuous with the lining membrane of the blood-vessels.

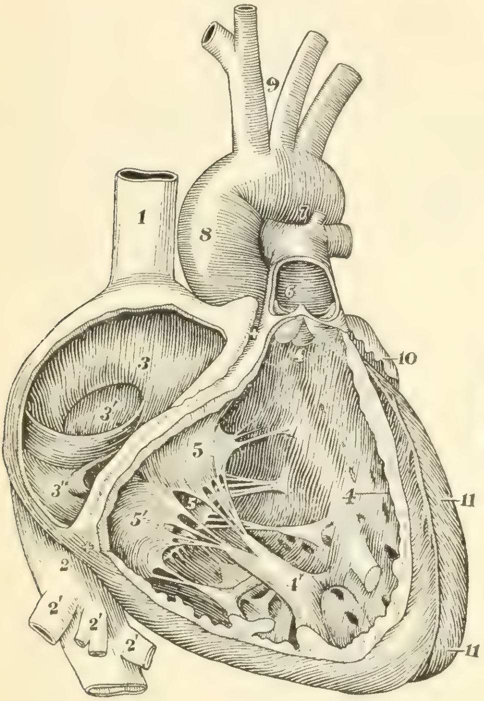

FIG. 111.

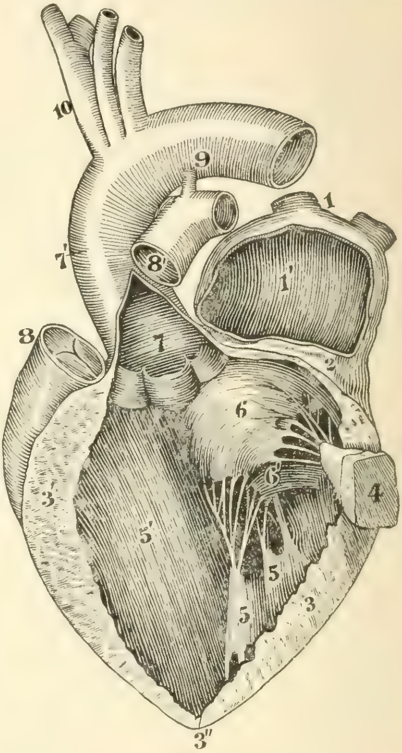

FIG. 112.

FIG. 111.—INTERIOR OF RIGHT AURICLE AND VENTRICLE, EXPOSED BY THE REMOVAL OF A PART OF THEIR WALLS. 1, Superior vena cava; 2, inferior vena cava; 2', hepatic veins; 3, 3', 3'', inner wall of right auricle; 4, 4, cavity of right ventricle; 4', papillary muscle; 5, 5', 5'', flaps of tricuspid valve; 6, pulmonic artery in the wall of which a window has been cut; 7, on aorta near the ductus arteriosus; 8, 9, aorta and its branches; 10, 11, left auricle and ventricle.—(*Allen Thomson.*)

FIG. 112.—LEFT AURICLE AND VENTRICLE, OPENED AND PART OF THEIR WALLS REMOVED TO SHOW THEIR CAVITIES. 1, Pulmonic vein cut short; 1', cavity of left auricle; 3, 3'', thick wall of left ventricle; 4, portion of the same with papillary muscle attached; 5, the other papillary muscles; 5', wall of the ventricle; 6, 6', the segments of the mitral valve; 7, the figure in aorta is placed over the semilunar valves; 7', aorta; 8, pulmonic artery; 10, branches of aorta.—(*Allen Thomson.*)

The inter-auricular septum is quite thin and composed of the two layers of the endocardium, between which is a layer of muscle-fibers. It presents at its lower portion an oval depression, the *fossa ovalis.*

The inter-ventricular septum is quite thick and well developed, and composed of the two layers of the endocardium enclosing the muscle-fibers. In the upper and central portion of the septum, there is, however, a small region which is thin owing to the absence of muscle-tissue and composed of endocardium only. This region is known as the *pars membranacea septi.*

The Cardio-pulmonic Vessels.—Though the two sides of the heart are separated from each other by the auriculo-ventricular septum, they are anatomically and physiologically connected by the intermediation of the pulmonic system of vessels: viz., the pulmonic artery, capillaries, and veins (Fig. 110).

The *pulmonic artery* arises from the conus arteriosus of the right ventricle. After a short upward course it divides into a right and a left branch, which enter the corresponding lungs. The vessel at once divides and subdivides into a number of branches, which, after following the bronchial tubes to their termination, give origin to capillaries that surround the air-cells of the pulmonic lobules.

The *capillaries* in this situation are extremely abundant and well developed. They lie close to the inner surfaces of the air-cells. The blood is thus brought into intimate relationship with the intra-pulmonic air, and the exchange of gases—the excretion of carbon dioxid and the absorption of oxygen—for which the cardio-pulmonic vessels exist, is readily accomplished.

The *pulmonic veins* which return the arterialized blood to the heart are formed by the convergence and union of the small veins which emerge from the capillary system. The final trunks thus formed, the four pulmonic veins—two from each lung—enter the posterior wall of the left auricle.

The Course of the Blood through the Heart.—There is thus established a pathway between the venæ cavæ on the right side and the aorta on the left side, by way of the right side of the heart, the cardio-pulmonic vessels, and the left side of the heart.

The venous blood flowing toward the heart is emptied by the superior and inferior vena cava into the right auricle, from which it passes through the auriculo-ventricular opening into the right ventricle (Fig. 110); thence into and through the pulmonic artery and its branches to the pulmonic capillaries, where it is arterialized by the exchange of gases—the giving up of a portion of carbon dioxid to the lungs and the absorption of oxygen—and changed in color from bluish-red to scarlet-red. The arterialized blood, flowing toward the heart, is emptied by the pulmonic veins into the left auricle, from which it passes through the auriculo-ventricular opening into the left ventricle; thence into the aorta and its branches to the systemic capillaries, where it is de-arterialized by a second but opposite exchange of gases—the giving up of a portion of its oxygen to the tissues and the absorption of carbon dioxid from the tissues—and changed in color from scarlet to bluish-red. The venous blood is again returned by the systemic veins to the venæ cavæ. Though the blood is thus described as flowing first through the right side and then through the left side, it must be kept in mind that the two sides fill synchronously; that while the blood is flowing into the right side from the venæ cavæ, it is also flowing into the left side from the pulmonic veins in equal quantities and velocities.

Though there is but one set of capillaries, as a rule, between arteries and veins, there is an exception in the case of the arteries and veins of some of the abdominal viscera. Thus the veins emerging from the capillaries of the stomach, intestines, pancreas, and spleen, instead of passing directly to the inferior vena cava, unite to form a large vein—the portal vein—which enters the liver. In this organ the portal vein divides to form a second capillary system which is in close relation to the liver cells and from which arise the veins which unite to form the hepatic veins. These latter vessels empty and discharge the blood into the inferior vena cava just below the diaphragm.

From the foregoing facts physiologists frequently divide the general circulation into:

1. The *pulmonic circulation*, which includes the course of the blood from the right side of the heart through the lungs to the left side of the heart.

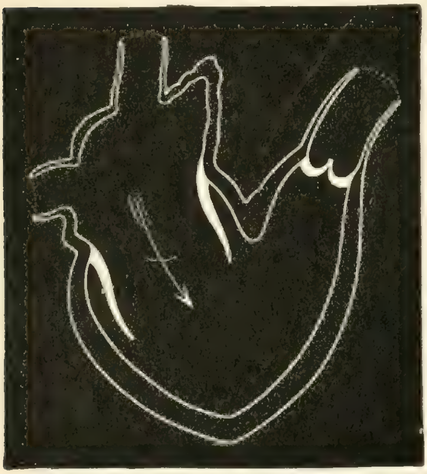

FIG. 113.—RIGHT CAVITIES OF THE HEART.—Auriculo-ventricular valve open, semilunar valves closed.—(*Dalton.*)

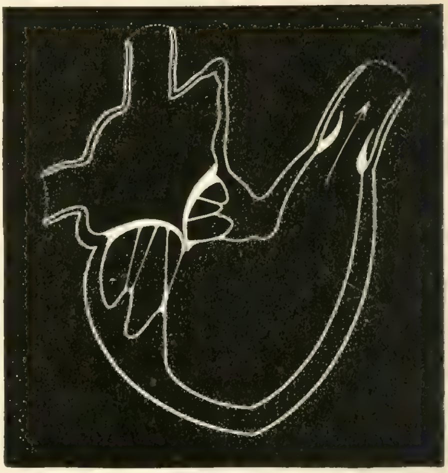

FIG. 114.—RIGHT CAVITIES OF THE HEART. Auriculo-ventricular valve closed, semilunar valves open.—(*Dalton.*)

2. The *systemic circulation*, which includes the course of the blood from the left side of the heart through the aorta and its branches, through the capillaries and veins, to the right side of the heart.
3. The *portal circulation*, which includes the course of the blood from the capillaries of the stomach, intestines, pancreas, and spleen through the portal vein, to the liver.

Orifices and Valves.—The movement of the blood along the path of the circle above outlined is accomplished by the alternate *contraction* and *relaxation* of the muscle walls of the heart. That the movement may be a progressive one, that there shall be no regurgitation during either the contraction or the relaxation, it is essential that some of the orifices of the heart be closed during each of these periods. This is accomplished by the heart valves.

The right auriculo-ventricular opening is surrounded and strengthened by a ring of fibrous tissue to which is attached a membrane partially subdivided into three portions or cusps, which during the period of relaxation are directed into the ventricle (Fig. 113); during the period of contraction they are raised and placed in complete apposition, when they act as a valve preventing a backward flow into the auricle (Fig. 114). In the former position the valve is open; in the latter, shut. For these reasons this structure is known as the *tricuspid valve.* This valve is formed of fibrous tissue derived from the fibrous ring, and some muscle-fibers, and covered over by a reduplication of the endocardium. To the under surface and to the edges of this valve the tendinous cords of the papillary muscles are firmly and intricately attached. These cords are just sufficiently long to permit closure of the valve and to prevent its being floated into the auricle.

The orifice of the pulmonic artery is also surrounded by a ring of fibrous tissue to which are attached three semilunar or pocket-shaped membranes, the semilunar valves. Each valve is formed by a reduplication of the endocardium strengthened by fibrous tissue. In the center of the free edge of the valve there is a small nodule of fibro-cartilage (the corpus Aurantii). The outer edge of the valve is strengthened by a delicate fibrous band. A similar band strengthens the convex attached portion of the valve just where it is joined to the fibrous ring. A third set of fibers pass toward the nodule, interlacing in all directions. Two narrow crescentic-shaped areas (the lunulæ) near the free edge are devoid of these fibers. During the period of *relaxation* of the heart the edges of the valves are in close apposition and prevent a return of the blood into the ventricle (Fig. 113); during the contraction they are directed into the artery (Fig. 114). In the former position they are shut; in the latter, they are open.

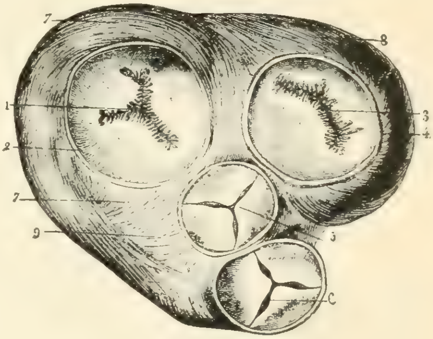

FIG. 115.—VALVES OF THE HEART. 1. Right auriculo-ventricular orifice, closed by the tricuspid valve. 2. Fibrous ring. 3. Left auriculo-ventricular orifice, closed by the mitral valve. 4. Fibrous ring. 5. Aortic orifice and valves. 6. Pulmonic orifice and valves. 7, 8, 9. Muscular fibers.—(*Bonamy and Beau.*)

The left auriculo-ventricular opening is provided with a similar though better developed fibrous ring and membranous valve. It is, however, subdivided into but two portions or cusps, and is therefore termed the *bicuspid valve*, or, from its fancied resemblance to a bishop's mitre, the *mitral valve.* The general arrangement, connections, and mode of action of this valve are similar in all respects to those of the tricuspid valve. The orifice of the aorta is also surrounded by a ring of fibrous tissue to which are attached three semilunar or pocket-shaped valves (Fig. 112), which in their arrangement, connections, and mode of action are similar in all respects to those at the orifice of the pulmonic artery. The anatomic relations of the cardiac orifices one to the other and the appearance presented by the valves when closed are represented in Fig. 115.

The Heart Muscle-fibers and Their Arrangement.—The muscle-fibers of the heart represent in their structure a type between the ordinary striated muscle and the smooth muscle. A longitudinal section of the heart-muscle shows a reticulated arrangement of the fibers, the outcome of a similar reticulated condition of the mesodermic material in which they develop. The mesodermic reticulum containing numerous nuclei is termed a syncytium. As the heart develops the muscle-fibers make their appearance in the protoplasm and assume an arrangement which corresponds to that of the trabeculæ composing the reticulum (Fig. 116). In the adult heart the intermediary spaces are reduced to narrow clefts in consequence of the multiplication of the muscle-fibers. The clefts are occupied with connective tissue, blood-vessels, lymphatics, etc. The individual fiber consists of alternate dim and light bands similar to the corresponding bands of the ordinary skeletal muscles, though it is devoid of a sarcolemma. Among the fibers large oval nuclei are distributed. At varying intervals the fibers are interrupted by intercalated discs. When the heart muscle is treated with caustic potash the trabeculæ separate at the level of these discs, forming what has hitherto been termed the muscle cell or fiber.

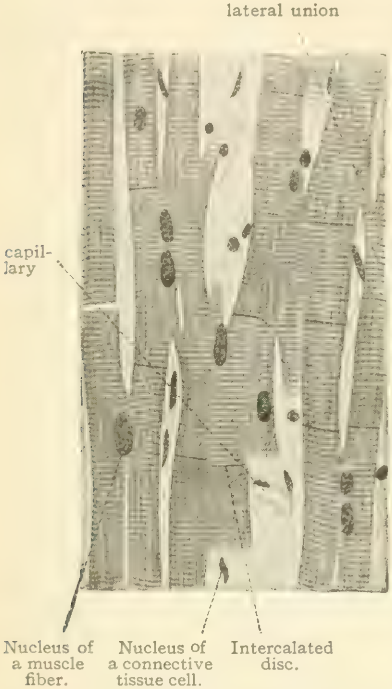
lateral union
capil-lary
Nucleus of a muscle fiber.
Nucleus of a connective tissue cell.
Intercalated disc.

Fig. 116.—From a Longitudinal Section of a papillary Muscle of the Human Heart. × 360.—(*Stöhr.*)

The arrangement of the muscle-fibers is quite complicated and in accordance with the functions of the individual portions of the heart. In the auricles the fibers are arranged in two sets: an outer transverse set, which pass from auricle to auricle, and an inner longitudinal set, which pass over the auricles and are attached anteriorly and posteriorly to the connective tissue of the transverse auriculo-ventricular septum. The longitudinal fibers of the auricles are practically independent of each other. Circularly arranged fibers are present near the terminations of the venæ cavæ and pulmonic veins.

In the ventricles the muscle-fibers are also arranged in two sets, a superficial longitudinal and a deep transverse, though their arrangement is somewhat more complicated than that observed in the auricles. In a general way it may be said that the superficial longitudinal fibers on both the anterior and posterior surfaces take their origin in the connective tissue of the auriculo-ventricular septum. The superficial fibers on the anterior surface of the heart pass obliquely downward and forward from right to left toward the apex, where they turn backward and inward in a vertical manner after which they ascend to terminate in the wall of the septum, the columnæ carneæ and musculi papillares. The superficial fibers of the posterior surface of the heart pass obliquely downward from left to right, wind around the apex, turn upward and end in the same structures as do the fibers from the anterior surface. The fibers from the base of the right ventricle terminate in the structures of the left ventricle, while those from the left ventricle terminate in the structures of the right ventricle. Longitudinal fibers are also found on the inner surface. The transverse fibers are very abundant and surround each ventricle separately though they are continuous with each other across the septum. Between the superficial longitudinal and deep transverse fibers there are several layers of fibers which possess varying degrees of obliquity. The general arrangement of the fibers is such as to insure a complete and simultaneous discharge of blood from both auricles as well as from both ventricles (Fig. 117).

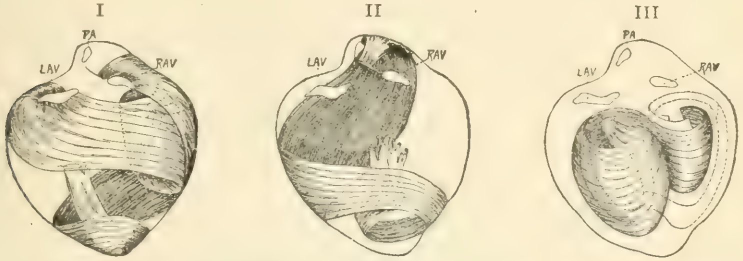

Fig. 117.—Arrangement of Ventricular Muscle-fibers.—(*After MacCallum.*) I and II, Superficial fibers of the left ventricle and conus arteriosus; III, deep layers of the left ventricle; LAV, mitral orifice; RAV, tricuspid orifice; PA, pulmonic artery.—(*From Hirschfelder.*)

THE MUSCLE CONNECTION BETWEEN THE AURICLES AND VENTRICLES

The Muscle Band of His, or the Auriculo-ventricular Bundle.—In the mammalian heart there is no continuity of the muscle-fibers across the auriculo-ventricular groove, uniting auricles and ventricles, such as exists in the frog or turtle heart. The muscle-fibers of the auricles and ventricles are completely separated from each other by the transverse fibrous septum to which they are attached. This fact has for a long time made it difficult to understand how the contraction process which begins in the auricles (and to which there will be occasion to refer in subsequent paragraphs) is conducted to the ventricles. The physiologic necessity for the existence of a muscle connection between the auricles and ventricles led to a series of investigations which have resulted in the discovery of an elaborate system of muscle-fibers by which they are united both anatomically and physiologically.

In 1893 Wilhelm His, Jr., discovered the existence of a band or bundle of muscle-fibers which apparently took its origin from the posterior part of the right side of the auricular septum, from which point it passed forward just above the auriculo-ventricular septum to a point near the aortic opening, where it divided into two portions, a right and a left, of which the latter apparently ended in the basis of the aortic leaflet of the mitral valve. This bundle has been termed "the muscle-bundle of His." In 1904 Retzer and Bräunig, working independently, corroborated the existence of this bundle and described its anatomic course more completely. The investigations of Bräunig led to the conclusion that this bundle of muscle-fibers which was constantly present in all animals examined, including man, began on the right side of the auricular wall below the fossa ovalis, from which point it passed forward, and anteriorly penetrated the auriculo-ventricular septum to become connected with the musculature of the ventricular septum just below the *pars membranacea septi.* Though both these observers state that the bundle divides into a right and left limb as it enters the ventricular septum, the ultimate distribution and termination of these limbs was not clearly determined. Retzer estimated that this bundle was 18 mm. long, 2.5 mm. broad, and 1.5 mm. thick. By these investigators this bundle was termed the "auriculo-ventricular bundle."

In 1906 Tawara published the results of an extended series of investigations made on the embryonic and adult hearts of many mammals including man, which resulted in a further increase of knowledge concerning the development, anatomic course, and histologic features of this bundle, and established beyond doubt that it is the pathway along which the contraction process is conducted from the auricles to the ventricles.

A brief summary of Tawara's account of this bundle is as follows: It arises near the opening of the coronary sinus where it is connected with the true auricular fibers. From their origin the fibers converge to form a distinct bundle which then passes forward on the right side of the auricular septum between the lower edge of the fossa ovalis and the auriculo-ventricular septum; just above the insertion of the median cusp of the tricuspid valve the bundle presents a very complicated network of muscle-fibers which has been designated as a knot or the auriculo-ventricular node or the node of Tawara; from the anterior portion of the node a bundle of fibers turns downward and penetrates the auriculo-ventricular septum, beyond which it passes below the *pars membranacea septi* to the upper limit of the muscle portion of the ventricular septum. It then divides into two limbs or branches which descend on either side of the septum under the endocardium, the right limb lying somewhat deeper than the left. Each of these limbs is enclosed by a layer of connective tissue which isolates it from the musculature of the ventricular septum as far as the lower third of the ventricular cavities. In this region they divide into a number of bundles, some of which enter the papillary muscles, while others, forming tendon-like strands, branch freely beneath the endocardium and spread in all directions over the entire inner surface of the ventricle and enter into histologic connection with the true cardiac muscle-fibers.

The fibers composing this system, and termed by Tawara from its supposed function the "conduction system" are histologically different from the cardiac fibers, in so far as they are poorer in sarcoplasm and similar in their appearance to embryonic muscle-fibers. In the auricular portion of the bundle the fibers exhibit a more or less reticular arrangement; in the ventricular portion, the fibers are more regularly arranged, are richer in sarcoplasm and present a number of fibrillæ near their periphery. In association with the muscle-fibers composing the auriculo-ventricular bundle there is a special collection of nerve-cells and nerve-fibers. Their function is unknown.

The ultimate termination of the system, beneath the endocardium, constitutes the so-called Purkinje fiber layer. In the sheep, calf, and in other animals these fibers are abundant and readily recognized; though they are not so well developed, they are nevertheless present and extensively distributed in the human heart.

The Keith-Flack Node or the Sino-Auricular Node.—This is a small body, discovered by the investigators whose names it bears, situated in the sulcus terminalis "just below the fork formed by the junction of the upper surface of the auricular appendix with the superior vena cava." It appears to be a remnant of primitive muscle tissue at what was formerly the junction of the sinus venosus and the auricle. In its structure it resembles the auriculo-ventricular (Tawara's) node, in that it consists of peculiar muscle-fibers, nerve-cells, and nerve-fibers enclosed by connective tissue. It is also provided with an abundant blood-supply. In the human heart, the muscle-fibers of this remnant are striated, possess well marked and elongated nuclei and are plexiform in arrangement. From the node the muscle-fibers extend downward along the sulcus terminalis for about two centimeters. The thickness of the bundle is about two millimeters. Superiorly the node appears to be connected with or continuous with fibers in the superior vena cava; inferiorly it is connected with the true auricular fibers. The dissection of this node shows that the terminal branches of the vagi and sympathetic nerves are in histologic relation with the nerve-cells. The situation, structure and relations of this neuro-muscle node appear to justify the assumption that it is directly concerned in the initiation of the heart-beat.

THE MECHANICS OF THE HEART

Methods of Observation.—The movements of the heart, as well as many phenomena connected with the flow of blood through its cavities, have been determined by observation of, and experimentation on, the exposed heart of a mammal—*e.g.*, dog, cat, rabbit—supplemented and corrected by experiments on the heart in its normal relations. Valuable information as to the heart-beat and the influences which modify it has been obtained from experiments made on the isolated heart of the turtle, frog, and allied animals.

If the thorax of a dog, completely anesthetized, is opened and artificial respiration established, the heart will be observed in active movement inside the pericardium. If this sac is divided and turned aside, the heart will be fully exposed to view. At the normal rate of movement of the heart characteristic of the dog it will be almost impossible to determine either the succession of events or their duration. But by observing the heart under different conditions at different rates of movement and with instrumental aids, physiologists have succeeded not only in analyzing the movements, but in describing their sequence and in estimating their time duration.

Phenomena Observed.—From many observations and experiments it has been determined that the heart at each beat presents two distinct movements which alternate with each other in quick succession. One is the movement of contraction, or the systole, by which the blood contained within its cavities is ejected into the arteries—pulmonic artery and aorta; the other is the movement of relaxation, or the diastole, followed by a pause during which the cavities again fill up with blood from the venæ cavæ and pulmonic veins.

The contraction of any part of the heart is termed the *systole;* the relaxation, the *diastole.* As each side of the heart has two cavities the walls of which contract and relax in succession, it is customary to speak of an auricular systole and diastole, and a ventricular systole and diastole. As the two sides of the heart are in the same anatomic relation to each other, they contract and relax in the same periods of time.

It has also been ascertained that the contraction of the auricles and ventricles as well as their subsequent relaxations, though occurring with extreme rapidity, do not take place simultaneously but successively; that the contraction process passes over the heart in the form of a wave; that it begins, indeed, at the terminations of the great veins, viz., the *venæ cavæ*, then passes to and over the auricles, thence to and over the ventricles from base to apex with great rapidity, but occupying in these different regions unequal periods of time; that the relaxation immediately succeeds the contraction, in the same order, and that at the close of the ventricular relaxation there is a period during which the whole heart is in repose, passively filling with blood.

The immediate cause of the movement of the blood through the vessels is the contraction and relaxation of the muscle-walls of the heart, and more particularly of the walls of the ventricles, each of which plays alternately the part of a force-pump, and possibly to a slight extent of a suction-pump. The motive power is furnished by the heart itself, by the transformation of potential energy, stored up during the period of rest, into kinetic energy—*i.e.*, heat and mechanic motion.

Changes in Position and Form.—It is also apparent under the condition of the foregoing observation that the heart during each pulsation undergoes changes of both position and form. In the diastolic condition, during which the heart is in repose, the apex is directed obliquely downward and to the left; the body of the heart is enlarged and its walls relaxed. As the systole begins and reaches its maximum, the apex is tilted upward, the entire heart is rotated on its axis from left to right and forced forward by the expansion and elongation of the pulmonic artery and aorta. As the diastole begins and rapidly passes to its completion a reverse series of movements is presented, viz.: an ascent of the heart due to the recoil and shortening of the pulmonic artery and aorta, a rotation of the heart on its axis from right to left, and a fall of the apex. With the completion of this latter event, the heart for a brief period is in repose.

It is probable, however, that these movements are not permitted to the same extent in the unopened chest, for the following reasons: the heart is enclosed in the pericardium, is supported posteriorly by the expanded lungs, and both posteriorly and inferiorly by the diaphragm, all of which coöperate in keeping the heart, and more particularly the right ventricle, in close contact with the chest wall and limiting its movements. By means of needles inserted into the apex of the heart, through the chest walls, it has been shown by their slight movement that the apex is practically a fixed point.

In the diastolic condition the shape of the heart near the base is elliptic on cross-section, the long diameter extending from side to side. In the completed systolic condition the shape of the same cross-section approximates that of a circle. In passing from the diastolic to the systolic condition the transverse diameter diminishes while the antero-posterior diameter increases, and the whole heart becomes somewhat more conic in shape. It is questionable if the vertical diameter perceptibly shortens. During the systole the heart hardens, increases in convexity, and is more forcibly pressed against the chest wall. As this takes place suddenly, it gives rise to a marked vibration of the chest wall, known as—

The Cardiac Impulse.—This impulse is principally observed in the space between the fifth and sixth ribs about an inch internal to a line drawn vertically from the middle of the clavicle. The cardiac impulse is synchronous with the cardiac systole.

The cardiac impulse may be recorded with an appropriate apparatus known as a *cardiograph;* the record obtained with it is known as a *cardiogram.* A cardiograph consists of a tambour covered with a thin rubber membrane provided with a button. The tambour is supported by a metallic frame which permits of an easy and accurate adjustment of the button over the seat of the cardiac impulse. A rubber tube connects the cardiographic tambour with a second tambour provided with a recording lever and thus transmits all variations in the pressure of the air in the former to the latter.

When all adjustments are carefully made a tracing similar to that shown in Fig. 118 will be obtained, in which the slight elevation *a* represents the contraction of the auricle which, completing the filling of the ventricle, causes the apex of the heart to press more vigorously against the chest wall; *b–c* represents the contraction of the ventricles, at which moment the apex is suddenly and forcibly driven against the chest wall; *c–d* represents the systolic plateau, the time during which the ventricle is discharging blood into the aorta; *d–e* represents the relaxation of the ventricle; while *e–f* represents the time of the diastole, during which the heart cavities are enlarging with the incoming of a new volume of blood in consequence of which the heart is pressing against the chest walls. The systolic plateau is characterized by one or more elevations and depressions, the true cause of which is unknown.

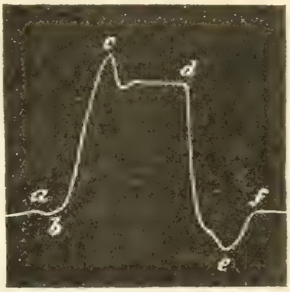

Fig. 118.—A Cardiogram.—(*After Pachon.*)

The Cardiac Cycle.—The term cardiac cycle is employed to express the sequence of events from the beginning of one auricular systole and the beginning of the auricular systole which immediately follows it. An examination of the heart shows that each pulsation may be divided into three phases, viz.:

1. The auricular systole.
2. The ventricular systole.
3. The pause or period of repose during which both auricles and ventricles are at rest.

The Graphic Record of the Cardiac Cycle.—For the purpose of obtaining accurate information as to the sequence of events, their time relations, as well as of the pressure within the heart cavities during each phase of its activity, it is necessary to obtain graphic records of the entire cardiac cycle.

This was first successfully accomplished by Chauveau and Marey, by means of sounds or tambours (Fig. 119) introduced through the jugular vein into the cavities of the right heart. Each tambour consists of a metallic frame covered by a thin rubber membrane. By means of flexible tubes, a. v., the interior of each tambour can be placed in communication with the interior of a second tambour provided with a recording lever. Pressure applied to the cardiac tambour will be followed by a movement of the enclosed air toward the recording tambour indicated by an outward movement of its membrane and a rise of the lever; removal of the pressure will be followed by a movement of the enclosed air toward the cardiac tambour indicated by an inward movement of the membrane and a fall of the lever.

When the tambours are introduced into, and carefully adjusted to the interior of the right heart, the auricular and ventricular contractions will exert pressure on their enclosed tambours as indicated by the rise of the levers of the recording tambours, which continues so long as the pressure lasts. With the relaxation of the auricular and ventricular walls the pressure is

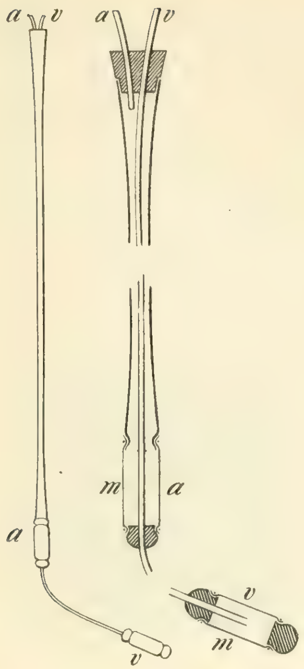

Fig. 119.—Cardiac Sounds. *v*, Tambours to be inserted into the ventricle; *a*, tambour to be inserted into the auricle; *m*, rubber membrane surrounding metal frame-work; *a*, *v*, ends of tubes in connection with tambours.—(*Marey*.)

removed and the levers fall to their former position. When the levers are applied to the surface of a recording cylinder a record of auricular and ventricular contractions is obtained such as that shown in Fig. 120.

A similar record would be obtained if the tambours were placed in the cavities of the left side of the heart.

In the graphic record, Fig. 120 obtained by the foregoing method, it is apparent that during the period of repose there is a gradual ascent of the tips of the recording levers, the result of a gradual increase of pressure due to the accumulation of blood within the heart cavities. When this reaches a certain level the auricular contraction occurs rather suddenly, followed by an equally sudden relaxation, after which the auricular walls remain at rest for a relatively long period, though the pressure within the auricle undergoes variations both in the way of increase and decrease as shown by small undulations on the curve.

With the close of the auricular systole, the ventricular systole occurs quickly and energetically and endures for some time, after which the ventricular walls quickly relax and remain at rest until the close of the next auricular contraction. The summit of the ventricular tracing generally spoken of as the *plateau* presents a series of elevations and depressions as stated in a foregoing paragraph.

A comparison of the two traces shows that between the close of the auricular and the beginning of the ventricular systole there is a slight pause known as the *intersystolic pause* (Chauveau). The tracings also show that between the close of the ventricular contraction and the beginning of the succeeding auricular contraction there is a period during which the whole heart is at rest and during which the cavities are filling with blood.

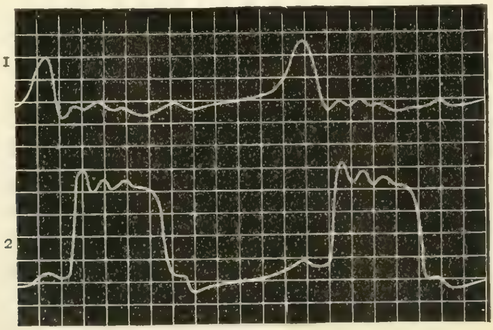

Fig. 120.—A Graphic Record of (1) the Intra-auricular Pressure; and (2) the Intra-ventricular Pressure of the Horse.—(*Chauveau and Marey*.)

For the purpose of obtaining the time of all these events, the recording surface was divided into equal spaces by vertically drawn lines. The rate of movement of the surface was such that each division corresponded to one-tenth of a second. The record thus indicates that the auricular contraction lasted approximately 0.2 second, the ventricular contraction 0.4 second, and the pause 0.4 to 0.6 second.

From similar experiments made on other animals, *e.g.*, the dog, similar results have been obtained; but by reason of the employment of more sensitive and more quickly responsive tambours, the curve of the auricular contraction exhibits variations not recorded by the forms of tambour used in earlier experiments. Reference to these variations will be alluded to in subsequent paragraphs. The results obtained by recent observers now generally accepted are in accord with the results obtained by Chauveau and Marey by means of their cardiac tambours as shown in Fig. 120.

The Movement of the Blood During the Cycle.—From the characteristic features of the foregoing record it is apparent that with the relaxation of the auricular walls, blood at once flows from the venæ cavæ and the pulmonic veins into the auricular cavities and continues so to do throughout the entire auricular diastole. With the relaxation of the ventricular walls, however, the blood that has accumulated in the auricles up to this time, or its equivalent coming from the venæ cavæ and pulmonic veins, now flows into the ventricles until they are nearly filled. Before they are filled, however, the auricular diastole comes to an end, the auricular walls again contract and force some of their contained blood into the ventricles and thus rapidly complete the filling. The ventricular systole immediately follows, during which the blood is driven into the pulmonic artery and aorta. This having been accomplished, the ventricles relax, and the blood that has been accumulating in the auricles begins to flow into the ventricles, after which the same series of events follows as in the previous cycle.

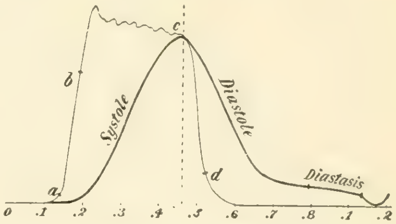

Fig. 121.—The Volume Curve of the Heart Contrasted with the Curve of the Intraventricular Pressure.

The Curve of the Systole and Diastole of the Heart.—In the study of the volume changes of the heart by means of a specially devised cardiometer, Henderson was enabled to record the contraction and relaxation movements of the heart, obtaining thereby a curve that resembled the curve of the contraction and relaxation of a skeletal muscle. If this curve is reversed and superposed on a curve of the intra-ventricular pressure, their relation one to an other becomes apparent, Fig. 121.

The chief characteristic of the systolic portion of the curve, viz.: its steep ascent, though less than that of the pressure curve, shows that with the opening of the semilunar valves, b, a large portion of the volume of the blood in the ventricles, 90 per cent. according to Henderson, is quickly and in a uniform manner discharged, after which the outflow slows and finally ceases as indicated by the rounded apex of the curve. The chief characteristic of the diastolic portion of the curve, viz.: its steep descent, though less than that of the pressure curve, shows that with the opening of the auriculo-ventricular valves, *d*, a large portion of the volume of the blood in the auricles flows quickly into the ventricles during the early part of the diastole, nearly, if not entirely refilling them, a procedure occupying a period of time approximately that required for the systolic discharge. In some experiments the portion of the curve, recording the increase of volume does not reach the abscissa but runs off parallel with it. In other experiments it gradually approximates the abscissa or shows a slight fall at the time of the succeeding auricular contraction. According to Henderson blood has ceased to flow from the auricles into the ventricles during the foregoing period and the contraction of the auricles adds but little to the volume of the blood already in the ventricles. Other investigators attach more importance to this event.

The portion of the volume curve between the apex and the beginning of the succeeding ventricular systole, embracing the entire diastolic period, has been subdivided into two portions, viz.: (*a*) from the apex to the beginning of the horizontal portion, corresponding to the period of relaxation and refilling—the diastole proper—and (*b*) the period of rest or the diastasis. This latter period is of rather short duration in the normal rate of heart beat. It lengthens if the rate decreases, and shortens if the rate increases.

The Action of the Valves During the Cycle.—As previously stated, the forward movement of the blood is permitted and regurgitation prevented by the alternate action of the semilunar and the auriculo-ventricular valves. As a point of departure for a consideration of the action of the valves and their relation to the systole and diastole of the heart, the close of the ventricular systole may be conveniently selected.

At this moment, if the blood is not to be returned to the ventricles, the *semilunar valves* must be instantly and completely closed. This is accomplished in the following manner: During the outflow of blood from the ventricles the valves are pushed outward toward the walls of the vessels, though not coming into contact with them, for behind them are the pouches of Valsalva, containing blood, continuous with and under the same pressure as that in the vessels themselves. With the cessation of the outflow and the beginning of the relaxation the pressure of the blood behind the valves suddenly forces them inward until their free edges, including the lunulæ, come into complete apposition. By this means the orifices of the pulmonic artery and aorta are securely closed and a return flow prevented. Reversal of the valves is prevented by their mode of attachment to the fibrous rings of the orifices.

During the ventricular systole the relaxed auricles have been filling with blood. With the ventricular *relaxation* this volume, or its equivalent, flows readily into the empty and easily distensible ventricles, its place being taken by an additional volume of blood flowing from the venæ cavæ and pulmonic veins. Whether the ventricles exert a suction power at the moment of their relaxation is an undecided question. A steady stream of blood into the auricles and ventricles continues throughout the entire period of rest until both cavities are filled. The tricuspid and bicuspid valves which hang down into the ventricular cavities are now floated up by currents of blood welling up behind them until they are nearly closed. The auricles now contract, forcing their contained volumes, or at least the larger portions of them, into the ventricles, which become fully distended.

With the cessation of the auricular systole the ventricular systole begins. If the blood is not to be returned to the auricles at this moment, the *tricuspid* and *mitral* valves must be suddenly and accurately closed. This is readily accomplished by reason of the position of the valves, which have been floated up and placed almost in apposition by the blood itself. With the beginning of the ventricular pressure the blood is forced upward against the valves until their free edges are brought together and the orifices closed. Reversal of these valves into the auricles is prevented by their attachment to the *chordæ tendineæ*, and the latter are kept from moving bodily upward during the ventricular contraction by the compensatory downward pull of the *papillary muscles.* The blood now confined in the ventricle between the closed auriculo-ventricular and semilunar valves is subjected to pressure from all sides. As the pressure rises proportionately to the vigor of the contraction, there comes a moment when the *intra-ventricular* pressure exceeds the pressure in the aorta and in the pulmonic artery. As soon as this occurs the semilunar valves of both vessels are thrown open and the blood discharged.[1] Both contraction and outflow continue until the ventricles are practically empty, after which ventricular relaxation sets in. With the discharge of the blood the pressure in both the pulmonic artery and aorta rises, passing from a minimal to a maximal value. Coincidently the pressure in the ventricles rises and even exceeds that in the pulmonic artery and aorta and so continues until near the close of the systole when the two opposing pressures are approximately equal. With the onset of the ventricular relaxation the intra-ventricular pressure suddenly falls, and so soon as it falls below the positive pressure of the blood in the sinuses of Valsalva the semilunar valves are again closed, the column of blood is supported, and regurgitation is prevented. In the meantime and while the ventricles are contracting, blood is again flowing into, and accumulating in the auricles and thereby distending them preparatory to the next systole. With the accumulation of blood in the auricles and ventricles the cardiac cycle is completed.

The approximate changes in the shape of the heart, the variations in the size of its cavities and in the size of the blood-vessels arising from them, and the relative position of the valves during systole and diastole are shown in Fig. 123.

Heart-sounds.—Two sounds accompany each pulsation of the heart, both of which may be heard by applying the ear or the stethoscope to the chest walls, especially over the region of the heart. One of these sounds is low in pitch, dull and prolonged; the other is high in pitch, clear and short. These sounds can be approximately reproduced by pronouncing the syllables *lūbb-dŭp, lūbbdŭp.* The long dull sound occurs with the systole, the first phase of a new cardiac cycle, and is therefore termed the *first sound;* the short clear sound occurs at the beginning of the diastole, with the second phase of the cardiac cycle, and is therefore termed the *second sound.* The first sound is the systolic, the second the diastolic. With the ear it can readily be determined that there is a brief pause between the first and second sounds, and a longer pause between the second and the first sounds. The duration of the first sound is almost equal to the duration of the systole—viz., 0.3 second; the duration of the second sound is not more than 0.1 second. The systolic sound is heard most distinctly over the body of the heart; the diastolic sound is heard most distinctly in the neighborhood of the third rib to the right of the sternum.

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[1] The discharge of the blood by the contraction of the ventricular walls is probably aided by the simultaneous downward displacement of the more central portion of the auriculo-ventricular septum, due to the contraction of the papillary muscles.

The *causes* of the heart-sounds have enlisted the attention of clinicians and physiologists for years, and many factors have been assigned for their production. At present it is generally believed that the *first sound* is the product of at least two, possibly three, factors: viz., the contraction of the muscle walls of the ventricles, the simultaneous closure and subsequent vibration of the tricuspid and mitral valves, and the sudden increase of pressure of the apex of the heart against the chest wall.

That the contraction of the ventricular muscle gives rise to a sound is certain from the fact that it is perceptible in an excised heart when the cavities are free from blood and when the valves are prevented from closing. The explanation of this sound is extremely difficult, as the contraction, though prolonged, is not of the nature of a tetanus and therefore not characterized by rapid variations of tension. The apex element may be eliminated by placing the individual in the recumbent position.

The *second sound* is the product of the simultaneous closure and subsequent vibration of the aortic and pulmonic valves which occur at the beginning of the ventricular diastole as the blood surges back against the closed valves. This has been definitely proved by the fact that the sound disappears when the valves are destroyed or held back by hooks introduced into the aorta and pulmonary artery. It is also possible that the vibration of the column of blood produces an additional tone which adds itself to that produced by the valves.

The foregoing events are shown in their order in the following diagram.

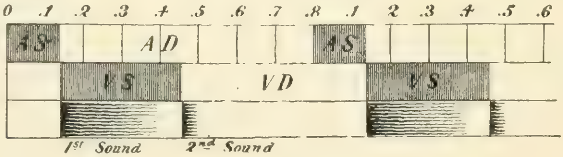
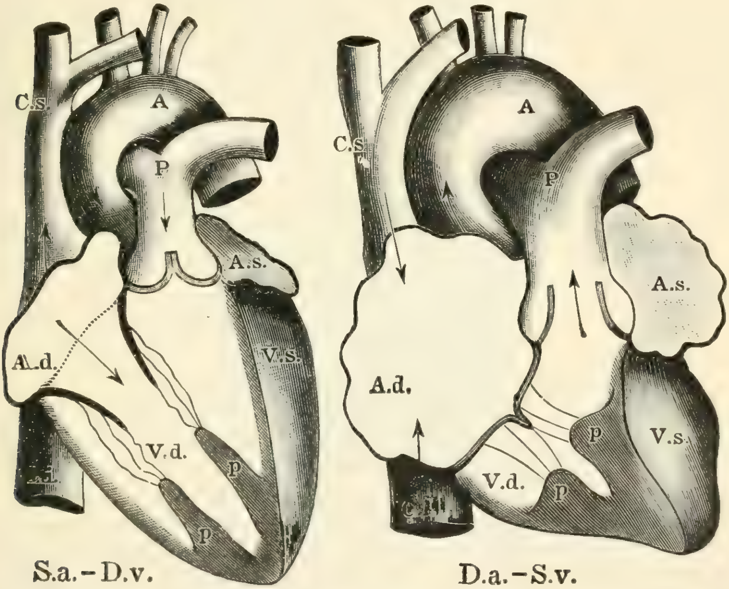


FIG. 122.—DIAGRAM SHOWING THE EVENT IN THE CARDIAC CYCLE.

Relative Functions of Auricles and Ventricles.—Though both auricles and ventricles are essential to the continuous movement of blood, they possess unequal values in this respect. The passage of the blood through the pulmonic and systemic vessels is accomplished by the driving power of the right and left ventricles respectively, aided, however, by minor extra-cardiac forces. They may be regarded therefore as *force-pumps*.

If the heart consisted of ventricles only, the flow of blood from the venæ cavæ and pulmonic veins would be temporarily arrested during their systole and their subsequent refilling delayed. This is obviated, however, by the addition of the auricles; for during the ventricular systole the blood continues to flow into the auricles, in which it is temporarily stored until the ventricular relaxation sets in. With this event the accumulated blood passes into the ventricles, which are thus practically filled before the auricular systole occurs by which the filling is completed. By this means there is no delay in the filling of the ventricles, and hence their effective working as force-pumps is more readily secured. The auricles may therefore be regarded as *feed-pumps*. For this reason it is probable, notwithstanding the contraction of the circular muscle-fibers at the terminations of the venous system, that the flow of blood into the auricles is never entirely arrested, but merely retarded. Regurgitation in these vessels does not occur for the reason that the retardation develops a side pressure during the auricular contraction which is equal to if it does not exceed the pressure in the auricle.

Synchronism of the Two Sides of the Heart.—If the balance of the circulation is to be maintained, the two sides of the heart must act synchronously. That they do so can be shown by attaching levers to their walls, and thus recording their activities. The synchronism is so perfect that until recently it was generally believed to be dependent on nerve connections; but Porter has shown that if the ventricles are cut away from the auricles, in which the nerve mechanism seems to lie, the synchronism of the former is not interfered with; that the apical halves of the ventricles will beat synchronously if perfused with blood through an artery; that a very small bridge of muscle-tissue will carry the wave of excitation from one part to neighboring parts of the ventricle. It is therefore probable that the synchronism is accomplished through muscle connections only. The left ventricle, in keeping with the greater work it has to do, has a greater development than the right, and therefore contracts more energetically. The ratio between the energy of the left and right sides is approximately 3 to 1.



S.a.-D.v. **D.a.-S.v.**

FIG. 123.—DIAGRAMMATIC REPRESENTATION OF THE AURICULAR SYSTOLE, S.a., WITH THE VENTRICULAR DIASTOLE, D. v., AND OF THE AURICULAR DIASTOLE, D. a., WITH THE VENTRICULAR SYSTOLE, S.v. C.s. and C.i. Superior and inferior cavæ; A.d. (atrium dextrum) right auricle; A.s. (atrium sinistrum) left auricle; V.d. (ventriculus dexter) right ventricle; V.s. (ventriculus sinister) left ventricle; P. pulmonic artery; A. aorta; P.P. papillary muscles.—(*Landois.*)

Intra-ventricular Pressure.—1. *Positive Pressure.*—It has been stated that during the pause of the heart when its cavities are filling with blood the semilunar valves are kept closed by the pressure of the blood in the pulmonic artery and aorta, a pressure due to the resistance, as will be explained later, offered to the flow of the blood mainly by the smaller arteries and capillaries; that they are opened only when the pressure of the blood within the ventricle exceeds that in the arteries. It is apparent therefore that there must be, during the time of the systole, an intraventricular positive pressure sufficiently high to overcome and even exceed the pressure ordinarily present in the aorta and pulmonic artery. It becomes, therefore, a matter of interest to determine the extent of this pressure as well as its variations during the course of a cardiac cycle. This can be done by inserting a long catheter into either the right or left ventricle, through the jugular vein, or the carotid artery respectively, and connecting its free extremity with a mercurial manometer. By the interposition of a double valve such as represented in Fig. 124, it becomes possible, according to the direction in which the blood is permitted to flow, to obtain either the maximal or the minimal pressure that occurs in the heart during a series of cycles. By the employment of a device of this character Goltz found in the left ventricle of the dog a maximal pressure of 114 to 135 mm. of mercury; in the right ventricle, a maximal pressure of 35 to 62 mm.

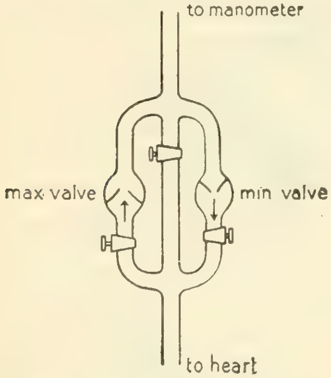


FIG. 124.—V. FRANK'S VALVE. This is placed in the course of the tube between heart and manometer, so that the latter may be used as a maximum, minimum, or ordinary manometer according to the tap which is left open.—(*Starling.*)

The maximal pressure in the ventricles during the systole, though always higher than that in the arteries, is neither a fixed nor an invariable pressure, as it rises and falls with the latter from moment to moment. Within limits the cardiac power, and therefore the intra-ventricular pressure, is capable of considerable increase. The function of the heart is to drive the blood through the vessels with a given velocity. This is possible only by first overcoming the resistance to the flow offered by the vessels, as indicated by the arterial pressure. As this is a variable factor, rising and falling very considerably at times, the heart must meet and exceed each rise, within limits if the circulation is to be maintained. This it does by calling on the reserve power with which it is endowed. The power put forth by the heart is proportional to the work it has to perform. If the arterial pressure continues higher than the average for any length of time, the heart meets the condition by an hypertrophy of its walls, but in so doing it encroaches on the reserve power proportionally and when the latter has become exhausted the heart may, on some sudden rise of pressure in the aorta, be unequal to the discharge of blood from its cavities and hence remain in a state of permanent diastole.

2. *Negative Pressure.*—It has also been demonstrated by the employment of the minimal valve that there is brief moment in the cycle when the

intra-ventricular pressure is less than the pressure of the atmosphere, becoming indeed negative to it. This moment must be that between the beginning of the relaxation of the ventricles and the opening of the auriculo-ventricular valves. The extent of the negativity, its duration and frequency have never been satisfactorily determined. Goltz, however, found in the left ventricle of the dog a minimal pressure of −23 to −50 mm. of mercury. The cause of the negative pressure, its influence on the opening of the auriculo-ventricular valves, and on the entrance of blood into the ventricles are equally unknown. A probable cause is an expansion of the base of the ventricles due to the enlargement of the aorta and pulmonic artery. That it is not due to the expansion of the thorax is evident from the fact that it occurs when the thorax is open and the heart exposed.

The Intra-ventricular Pressure Curve of the Dog.—It was stated in a previous paragraph that the contraction of the auricles and ventricles of animals other than the horse have been graphically recorded. This is especially true of the heart of the dog. A graphic record of the intra-ventricular pressure, its course, its variations, and time relations is necessary for the interpretation of the heart mechanisms. With such a record may be compared the records of the pressures in the venæ cavæ and auricles on the one hand, and in the aorta, on the other hand, and their relations one to another accurately defined.

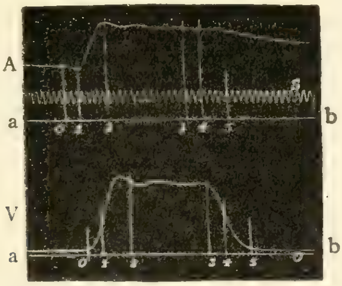


Fig. 125.—V. Curve of the Pressure in the Ventricle of the Dog. A. Curve of the Pressure in the Aorta. The curves were taken simultaneously. *s*, Tuning-fork vibrations each corresponding to 1/100 of a second. a–b, line of atmospheric pressure. The ordinates 0–5 correspond in the two records. 0, Closure of the auriculo-ventricular valve; 1, opening of the semilunar valves; 2, point of maximum pressure; 3, beginning of the ventricular relaxation; 4, closure of the semilunar valves; 5, opening of the auriclo-ventricular valve. (*Hürthle.*)

The intra-ventricular pressure has been obtained by specially devised manometers or *tonometers* or *tonographs*, as they are variously termed, the construction of which is such as to enable them to respond instantly to the very rapid variations of the pressure which occur during the brief cardiac cycle. One of the best is that of Hürthle. This consists of a small metallic tambour 5 or 6 millimeters in diameter, covered by a thin rubber membrane. A small button resting on the membrane plays against an elastic steel spring, by the tension of which the pressure of the blood is counterbalanced. The movements of the membrane are taken up, magnified, and recorded by a suitable lever. A long cannula is inserted into the right ventricle through the jugular vein or into the left ventricle through the carotid artery. Both cannula and tambour are filled with an alkaline solution to prevent coagulation of the blood, and then made air-tight. The pressure of the blood in the ventricle is thus transmitted by a liquid column to the tambour and to its attached lever. With such a manometer a curve is registered similar to that shown in Fig. 125. To obtain the absolute value of this curve in millimeters of mercury it is necessary to graduate the instrument previously. An examination of the curve shows that previous to the ventricular contraction there is a very slight rise of pressure above that of the atmosphere, represented by the line *a—b*. This may be due to the inflow of blood from the auricle during the diastole. At 0 the pressure suddenly rises, passes quickly to its maximum value, (2), which is maintained with slight variations for some time, and then suddenly (3) begins to fall, and rapidly reaches the line of atmospheric pressure, or even passes below it, becoming negative in fact for a short period. The curve may also be taken as a record of the ventricular contraction, for there are reasons to believe that the two closely coincide throughout their entire course. A characteristic feature of this curve is the more or less horizontal portion comprised between the points 2 and 3, marked by several elevations and depressions, which has been termed the *systolic plateau.*

With other forms of elastic manometers, especially those in which the transmission of the intra-ventricular pressure is effected by air or by a combination of air and liquid, this portion of the curve is represented by a single peak, which is taken as an indication that the maximal pressure once reached is not maintained, but immediately begins to fall to its original level, notwithstanding the continued contraction of the ventricle. Those who adhere to this view attribute the plateau to the closure of the orifice of the catheter by the contracting and approximating walls of the ventricle. There are reasons for believing, however, that the former curve is the more correct representation of the course of the intra-ventricular pressure. Bayliss and Starling photographed on a moving surface the oscillations of a fluid, a solution of sodium sulphate, in a capillary glass tube one end of which was closed, the other end placed in connection with an intra-cardiac catheter, the oscillations representing the variations in pressure. The photogram thus obtained resembles the curve obtained by Hürthle's membrane manometer.

The Relation of the Intra-ventricular Pressure Curve to the Intracardiac Mechanisms.—By itself the curve of the intra-ventricular pressure affords no indication as to events occurring within the heart: *i.e.*, as to the times during the systole, of the closure of the auriculo-ventricular valves and the opening of the semilunar valves, or the times during the diastole, of the closure of the semilunar valves and the opening of the auriculo-ventricular valves.

By registering the curve of pressure in the aorta simultaneously with the pressure in the left ventricle (Fig. 125), and by comparing these with the curve of the successive differences of pressure in these two cavities as determined by the "differential manometer," it becomes possible to mark on the ventricular pressure curve the points at which the foregoing events take place. As the outcome of many observations and determinations, the following statements may be made: As a point of departure for a consideration of the relation of the intra-ventricular pressure to the time of action of the valves, the close of the ventricular systole may be conveniently selected.

During the systolic plateau the blood is passing from the ventricle into the aorta. Independent of the slight elevations and depressions there is an absolute fall of pressure between the beginning and the end of the plateau. There is also a corresponding fall in the aortic pressure, corresponding to these two points. The curve of the difference of pressure shows, however, that the ventricular pressure is slightly higher than the aortic. This fall in both ventricular and aortic pressures is due to the escape of blood from the arterial into and through the capillary system. At 3 (see Fig. 125), however, whether completely emptied or not, the ventricle suddenly relaxes, and its pressure soon falls below that in the aorta. As soon as this takes place the semilunar valves must close, if regurgitation into the ventricular cavity is to be prevented. A comparison of the aortic pressure curve shows a slight notch, the "dicrotic notch," just preceding a slight elevation, the "dicrotic" wave. This notch occurs at the moment when the semilunar valves close. The corresponding point on the ventricular pressure curve has been placed just where the ordinate 4 cuts the descending portion. As yet, however, the pressure is higher in the ventricle than in the auricle, and continues so until near the line of atmospheric pressure. At this point the pressure in the auricle, due to the accumulation of blood during the ventricular systole, now forces open the mitral valve and the blood flows into the ventricle. The opening of the mitral valve occurs about the point where the ordinate 5 cuts the curve.

The ventricular pressure curve affords but slight, if any, indication of the auricular systole. It apparently does not give rise to any noticeable increase in the ventricular pressure. The slight rise in the pressure curve, which just precedes the abrupt rise due to the ventricular systole, may be taken as an indication of an increasing pressure due to the inflow of blood from the auricle, as a result of the auricular systole. Immediately following this event the ventricular systole begins and as soon as the pressure in the ventricle exceeds that in the auricle the mitral valve closes. This is marked on the curve where the ordinate cuts it, at 0. With the closure of the mitral valve the blood becomes imprisoned within a closed cavity, closed at one orifice by the mitral valve and at the other orifice by the semilunar valves. As the blood is incompressible the intra-ventricular pressure under the force of the ventricular contraction rapidly rises and continues so to do until the pressure in the ventricle exceeds that in the aorta, at which moment the semilunar valves are suddenly opened and the blood discharged. A comparison of the aortic curve shows that for a short time during the ventricular systole the pressure is falling, but at one point the curve turns at a sharp angle and rapidly rises. This is an indication that the semilunar valves are suddenly thrown open and the blood begins to pass into the aorta. This event occurs at a moment marked on the ventricular curve by the ordinate 1. Beyond this point the pressure continues to rise, for the aortic pressure must not only be exceeded, but a certain velocity must be imparted to the blood. Between the ordinates 1 and 4, the semilunar valves remain open and the blood passes into the aorta.

In accordance with the foregoing: the ventricular systole may be subdivided into two periods:

1. The period of rising tension, from the beginning of the systole and the closure of the auriculo-ventricular valves to the opening of the semilunar valves, the *pre-sphygmic period*, occupying from 0.02 to 0.04 second.
2. The period of ejection, the *sphygmic-period*, from the opening of the semilunar valves to the end of the systole, occupying about 0.2 second.

The ventricular diastole may also be divided into two periods:

1. The period of falling tension or relaxation, the *post-sphygmic period*, from the end of the systole and the closure of the semilunar valves to the opening of the auriculo-ventricular valves, occupying about 0.05 second.
2. The period of filling, from the opening of the auriculo-ventricular valves to the beginning of the succeeding auricular systole.

The Time Relations of the Successive Periods of the Ventricular Activity of the Human Heart.—The duration of each of the periods of ventricular activity as stated in the foregoing paragraph holds true only for the animal the subject of the experiment. The time relations of each period vary somewhat with the animal as well as with the rate of the heart during the time of the experiment. In human beings the same holds true. As the outcome of different methods of investigation the average duration of each period has been approximately estimated as follows:

Period.	Rate 70.		Rate 80.	
1. Presphygmic	0.055	Systole 0.323	0.051	Systole 0.305
2. Sphygmic	0.268		0.254	
3. Post-sphygmic	0.050	Diastole 0.540	0.050	Diastole 0.445
4. Pause	0.490		0.395	
Total Duration	0.863		0.750	

The Intra-auricular Pressure.—During the auricular systole the pressure within the auricle undergoes variations as shown by direct examination by means of a cannula inserted into the auricular cavity and connected externally with a recording tambour, or by indirect examination by means of an exploratory tambour placed over the right jugular vein in close relation to the clavicle. The pressure variations in the jugular vein which are thus recorded by means of a tambour provided with a writing lever are believed to be caused by, closely follow and reproduce the pressure variations in the auricle.

Among the most important of the direct examinations of the auricular pressure are those of Porter, carried out by the insertion of a large cannula in the auricular appendix, or in a pulmonary vein close to the auricle and connected by its free extremity with a Hürthle tambour. The curve of pressure thus obtained, shown in Fig. 126,[1] is characterized by three positive and three negative waves. Among the more important of the indirect determinations of the auricular pressure variations are those of Bachmann, carried out with highly sensitive recording tambours. The curve of pressure variations in the jugular vein thus obtained, by Bachmann, Fig. 127, is placed in juxtaposition for purposes of comparison.

The *first positive* wave, *a*, is caused by the systole of the auricle and amounts to about 9 millimeters of mercury. The *first negative* wave is due to the relaxation of the auricle.

The *second positive* wave,[2] *s*, is not of auricular origin, but is due to the systole of the ventricle in its early stage corresponding to the period between the closure of the auriculo-ventricular valve, and the opening of the semilunar valves, the period of rising tension, and amounts to about 5 mm. of Hg. It is probably due to the bulging of the auriculo-ventricular valve into the auricular cavity, by the still higher ventricular pressure, thus diminishing its size and raising the pressure.

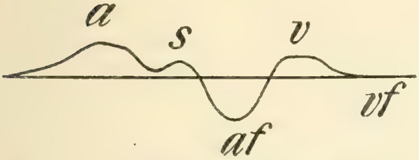


FIG. 126.—CURVE OF PRESSURE VARIATIONS IN THE AURICLES. (Enlarged.)—(*Porter.*)

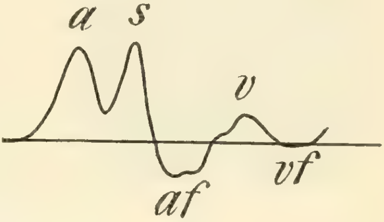


FIG. 127.—CURVE OF PRESSURE VARIATIONS IN THE JUGULAR VEIN. (Enlarged.)—(*Bachmann.*)

The *second negative* wave, *af*, begins with the opening of the semilunar valves, determined by comparison with a simultaneously recorded curve of intra-ventricular pressure, and is due in part to the relaxation of the auricular walls, but more especially to a descent of the more central portions of the auriculo-ventricular septum, into the ventricular cavity, due to the contraction of the papillary muscles during the ventricular systole. The hollow cone thus formed enlarges the auricular cavity, withdraws some of its contained blood, and hence lowers the pressure, thus contributing materially to the filling of the auricle. This negative pressure amounts to about −10 mm. of Hg.

The *third positive* wave, *v*, occurs toward the end of the ventricular systole and is probably caused by an inflow of blood from the veins as well as by a return of the auriculo-ventricular septum to its normal position, the result of a relaxation of the papillary muscles at a time when the intra-ventricular pressure is still higher than the intra-auricular pressure. It amounts to about 5 mm. of Hg.

The *third negative* wave, *vf*, appears very shortly after the relaxation of the ventricle and though there is at this moment a rapid fall of intra-ventricular pressure, on opening of the auriculo-ventricular valves and a descent of blood into the ventricle, the fall of auricular pressure seldom amounts to more than 0.5 mm. of Hg.

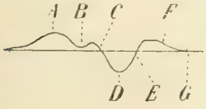


FIG. 128.—CURVE OF PRESSURE VARIATIONS IN THE AURICLE.—(*Porter.*)

[1] The original tracing obtained by Porter is shown in the accompanying Fig. 128. The letters designating the waves have the following significance. A, systolic rise; AB, first diastolic fall; BC, first diastolic rise; CD, second diastolic fall; E, second diastolic rise; F, third diastolic fall; G, pause. In Fig. 126 the tracing has been enlarged and the waves relettered and named in accordance with the terminology in vogue in the literature of clinical medicine.

[2] The corresponding wave on the curve of the pressure variations in the jugular vein is believed by Mackenzie to be due to the impact of the expanding carotid artery, and hence calls it the carotid, *c*, wave; inasmuch as it occurs in point of time with the beginning of the ventricular systole, it is also called the systolic, *s*, wave.

A Graphic Record of the Auricular and Ventricular Contractions of the Human Heart.—From the similarity of the anatomic arrangement of the human heart to that of mammals in general it is permissible to assume that a graphic record of the auricular and ventricular contractions of the human heart would resemble in its general features that of the hearts of mammals heretofore experimented on, and that the same series of events present themselves in the human heart during each cycle, though by reason of the difference in the rate of the beat, the duration of each event in the cycle is somewhat different.

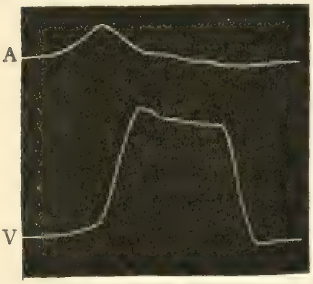


Fig. 129.—Tracings of the Auricular and Ventricular Contractions from a Woman with Ectopia of the Heart. *a*, Auricular; *v*, ventricular.—(*François-Franck.*)

The nearest approach to obtaining a graphic record of the auricular and ventricular contractions of the human heart by the direct application of exploratory tambours was made by François Franck on a woman whose heart was congenitally displaced into the abdominal cavity. An investigation revealed the fact that this woman had a large opening in the anterior portion of the diaphragm through which the ventricle had passed and formed a large protrusion in the epigastric region. Through thin and relaxed abdominal walls the ventricular pulsations could be distinctly felt as well as the pulsation of what appeared to be the inferior portion of the right auricle. A fibrous ring around the edge of the opening in the diaphragm supported the heart at the auriculo-ventricular groove. On the application of exploratory tambours in connection with recording tambours one to the right ventricle, the other to the right auricle, the record shown in Fig. 129 was obtained of which the upper line represents the contraction of the auricle and the lower line the contraction of the ventricle. A comparison of the record with that obtained from the horse, Fig. 120, p. 276, shows that the relation of the auricular to the ventricular systole is the same in the former as in the latter and that in their general features the two records correspond, from which it may be inferred that in the human heart the events occurring during the cycle are practically identical with those occurring in the hearts of other mammals. The small size of the auricular curve and the absence of undulations are probably due to the fact that the tambour was placed on only a portion of the auricle.

A Schematic Representation of the Events of a Cardiac Cycle in Man.—From graphic studies of the cardiac impulse, of the pressure changes in the auricle and ventricle as indicated by pressure changes in the jugular vein and carotid artery respectively it has become possible to construct a diagram of the cardiac cycle of the human heart, to designate on the ventricular curve the time of the opening and closing of the valves, as well as the time relations of the entire series of events. A scheme of this character is shown in Fig. 130, based on that constructed by Fredericq.

Though the numerical values given for the duration of the auricular and ventricular systole and diastole, viz.: auricular systole 0.10 second; auricular diastole 0.70 second; ventricular systole 0.33 second; ventricular diastole and pause 0.47 second, it must be borne in mind that they are true only for the heart beating approximately 75 times per minute. If the number of beats increases, not only does the entire cycle diminish in duration, but its different subdivisions, auricular systole, ventricular systole, and diastole also diminish in duration, though in unequal degrees. Thus it has been determined that with each increase of 10 beats above 70, the ventricular systole shortens by about 0.02 second and the ventricular diastole by about 0.10 second. The opposite holds true if the number of beats decreases below 70 per minute.

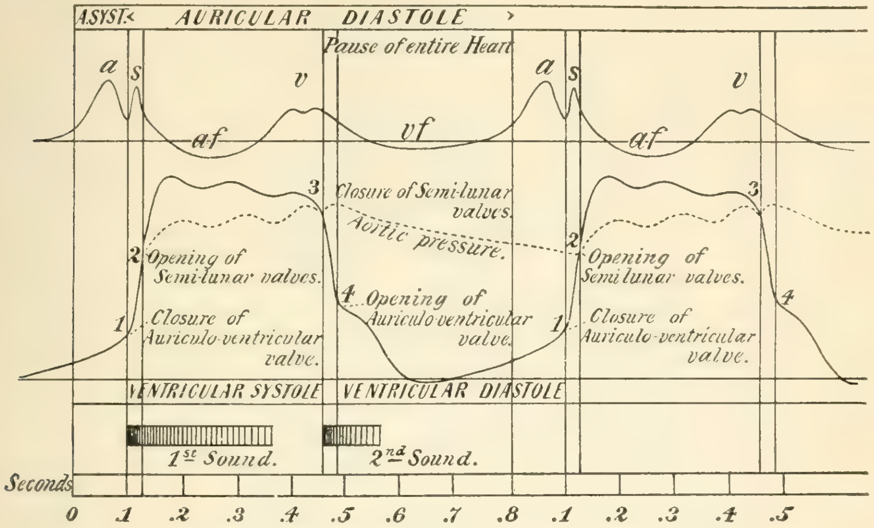

A.SYST.< AURICULAR DIASTOLE >
Pause of entire Heart
a
s
v
af
vf
a
s
v
af
3
Closure of Semi-lunar valves.
Aortic pressure.
2
Opening of Semi-lunar valves.
4
Opening of Auriculo-ventricular valve.
1
Closure of Auriculo-ventricular valve.
2
Opening of Semi lunar valves.
3
4
1
Closure of Auriculo-ventricular valve.
VENTRICULAR SYSTOLE
VENTRICULAR DIASTOLE
1st Sound.
2nd Sound.
Seconds
0 .1 .2 .3 .4 .5 .6 .7 .8 .1 .2 .3 .4 .5

FIG. 130.—A SCHEMATIC REPRESENTATION OF THE EVENTS OF A CARDIAC CYCLE.

The Relation of the Cardiogram to the Events of the Cardiac Cycle.—A comparison of a typical cardiogram, such as is seen in Figs. 118 and 131, with the curve of intraventricular pressure, shows that they correspond in essential features. The slight elevation (*a*) on the cardiogram represents the contraction of the auricle, which completing the filling of the ventricle causes it to press more vigorously against the chest wall; *b–c* represents the contraction of the ventricles, at which moment the apex is suddenly and forcibly driven against the chest wall; *c–d* represents the systolic plateau, the time during which the ventricle is discharging blood into the aorta; *d–e* represents the relaxation of the ventricle, while *e–f* represents the time of the diastole during which the heart cavities are enlarging with the incoming of a new volume of blood, in consequence of which the heart is pressing against the chest walls. The systolic plateau is characterized by one or more elevations and depressions, the true cause of which is unknown.

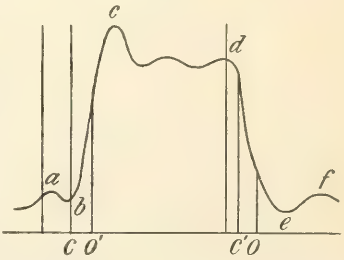


FIG. 131.—CARDIOGRAM. *a*, Auricular stysole; *b*, *c*, *d*, ventricular systole; *d*, *e*, ventricular diastole; *C*, *O*, closing and opening of the auriculo-ventricular valves; *O′*, *C′*, opening and closing of the semilunar valves; *C*, *O′*, period of rising tension; *O′D*, period of ventricular discharge; *C C′*, time of the occurrence of the first and second sounds respectively.

From the correspondence of the curve of cardiac pressure against the chest wall with the curve of intra-ventricular pressure it becomes possible to indicate with approximate accuracy the time of the opening and closing of the auriculo-ventricular valves and the semilunar valves and hence the time of occurrence of the heart sounds and other features of the cardiac cycle. Such a construction is shown in Fig. 131.

The Pulse Volume.—The pulse volume or the systolic output or the amount of blood discharged by the ventricle at each systole has long been a subject of investigation, but by reason of the inherent difficulties of the problem the results that have been obtained have varied within wide limits, viz.: from 180 c.c. to 50 c.c. The methods that have been employed for the determination of this volume are complicated and need not be detailed here. Suffice it to say that the results of the more recent experiments would indicate that the volume varies from 80 c.c. to 100 c.c. If the pulse volume be assumed to weigh 100 grams and the total volume of blood in a man weighing 70 kilograms to weigh 3864 grams then the pulse volume will be about one-thirty-eighth of the total weight of blood, or about 0.00142 of the body weight. In 38 heart beats therefore the entire amount of blood will have passed through the heart. The systolic output is conditioned by the factors which increase or decrease the length of the diastole and hence the filling of the ventricle.

The Frequency of the Heart-beat.—The frequency of the heart-beat varies with a variety of conditions: *e.g.*, age, sex, posture, exercise, etc.

Age.—The most important normal condition which modifies the activity of the heart is age. Thus:

Before birth, the number of beats a minute averages	140
During the first year it diminishes to	128
During the third year it diminishes to	95
From the eighth to the fourteenth year it averages	84
In adult males it averages	72

Sex.—The heart-beat is more rapid in females than in males. Thus while the average beat in males is 72, in females it is usually 8 or 10 beats more.

Posture.—Independent of muscle efforts the rate of the beat is influenced by posture. It has been found that when the body is changed from the lying to the sitting and to the standing position, the beat will vary as follows—from 66 to 71 to 81 on the average.

Exercise and *digestion* also temporarily increase the number of beats.

A *rise* in blood-pressure from any cause whatever is usually attended by a decrease, while a *fall* in blood-pressure is attended by an increase in the rate.

The Electric Currents of the Heart.—The wave of contraction of the heart muscle, like the wave of contraction of the skeletal muscle (see page 81) is accompanied or perhaps preceded by the development of electric currents the existence of which can be demonstrated by connecting the base and apex, by means of non-polarizable electrodes, with a suitable galvanometer. When the base and apex of the frog's heart are thus connected, it will be found that with each contraction, the galvanometer needle will deviate from its position of rest and in a direction that indicates that there is not only a change in their electric potential but also that the base becomes primarily electronegative to the apex which remains electropositive. With the development of the negativity a current passes down the heart to the apex, out through the galvanometer circuit and back to the point of origin. This current has been termed the *action* current.

If the heart is connected with a more quickly responsive apparatus, *e.g.*, a capillary electrometer (see appendix) it will be found that the mercury will pulsate twice, but in opposite directions, with each contraction, indicating that two action currents are developed, the *first* indicating that the base is primarily negative to the apex which is electropositive, and the *second* that the apex is secondarily negative to the base which has become again electropositive: in other words the changes in electric potential are *diphasic.* With the capillary electrometer Waller demonstrated that the human heart also exhibits similar changes in its electro-potential with each beat giving rise to electric currents which find their way through the surrounding tissues to the surface of the body from which they can be led off to the electrometer and then back to the surface of the body and finally to the base of the heart. He was enabled to determine and locate the points which are electronegative and electropositive. The results of his experiments are embodied in the accompanying diagram Fig. 132, which, with the legend is self-explanatory.

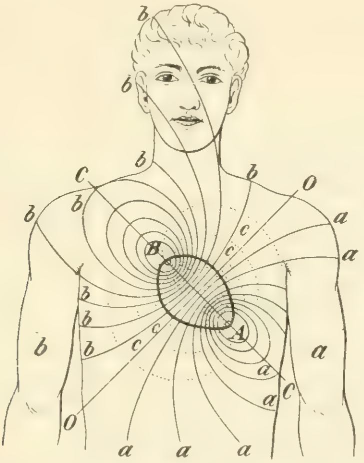


FIG. 132.—THE ELECTRONEGATIVE AND ELECTROPOSITIVE AREAS OF THE BODY SURFACE. *A* and *B* respectively represents apex and base of the ventricular mass. Then, if at any moment a difference of potential should arise between *A* and *B*, a current, *c c c*, will be established along and around the axis *C C*; the line *O O* will represent the plane of zero potential or equator; the lines *a a a*, *b b b* will represent equipotential curves around *A* and *B*. A difference of potential between *A* and *B* will be manifested if the two leading-off electrodes are applied on opposite sides of the equator, *O O*; no such difference will be manifested if both electrodes are on the same side of the equator. The equator *O O* will divide the body into two asymmetrical parts, (1) a portion *b b b* including the head and right upper extremity, (2) a portion *a a a* including the three other extremities.—(*Waller, Human Physiology.*)

If any two points, *a* and *b*, on opposite sides of the equator *O*, *O*, are connected with the electrometer the mercury will pulsate twice with each heart-beat indicating the presence of two action currents which travel successively in opposite directions. With suitable apparatus the oscillations of the mercury can be photographically recorded. By reason of the rapid action of the heart and the inertia of the mercury, the exact changes of the electric potential recorded are difficult of interpretation.

By means of the highly sensitive and quickly responsive string-galvanometer devised by Einthoven (see appendix) not only can the variations of the electric potential of the heart be detected, but the deviations of the string caused by the passage of the most delicate current, can be magnified and a shadow projected on a sensitive surface and photographed. The record thus obtained is termed.

The Electrocardiogram.—An electrocardiogram obtained by photographing the oscillations of the galvanometer string during the cardiac cycle, when different portions of the body surface, *a* and *b*, are connected with the terminals of the string, is shown in Fig. 133, the different features of which are designated by the letters *P*, *Q*, *R*, *S*, *T*. This curve, which represents the relative strength, duration, succession and direction of the currents during the cycle, it is believed furnishes a correct picture of the strength, duration, succession and direction of the physiologic processes—the excitation and contraction processes—as they arise in the heart muscle during its activity.

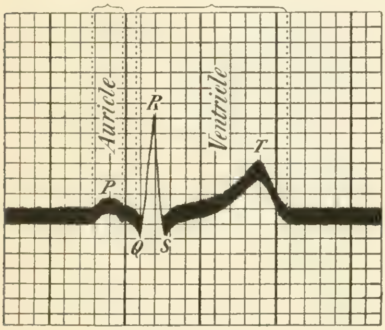


Fig. 133.—Scheme of the Electrocardiogram.—(*Einthoven.*)

The interpretations of the electrocardiogram and the significance of its various features are not, in some respects, in as complete accord as seems desirable. In general, it may be said that *P* corresponds to the auricular systole and that *Q*, *R*, *S*, *T* correspond to the ventricular systole. *R* and *T* are always present in physiological conditions at least, while *Q* and *S*, may, either one or the other or both, be wanting.

Einthoven is of the opinion that the general form of the electrocardiogram indicates the path and propagation of the stimulus or the excitation process through the heart, as well as the order of contraction of different portions of the ventricular walls, both of which are in harmony with the origin, course and ultimate distribution, of the auriculo-ventricular conduction system as determined by Tawara (see page 272).

The record presents first a horizontal portion—the image of the galvanometer string—which indicates that the string is at rest by reason of the fact that all portions of the heart, during the diastolic pause are isoelectric or of equal electropotential.

P is the result of the contraction of the auricle, indicating a condition of negativity toward the ventricle which is now electropositive in consequence of which, the electric currents pass down the heart, thence to the body surface, thence through the galvanometer circuit and back to the heart, causing the string as they pass through it, to move outward. With the cessation of the auricular contraction the string returns to its position of rest. The more or less horizontal line between *P* and *Q* indicates that both auricles and ventricles are now at rest and in the same state of electric potential. The passage of the excitation process through the conduction system, which is now taking place, from its beginning to its terminations, is, in and of itself, too feeble to cause a deviation of the thread under the conditions of tension necessary for the registration of the other features of the electrocardiogram.

The system of points or waves, negative and positive, *Q*, *R*, *S* in the first part of the ventricular portion of the electrocardiogram permits of the inference that the stimulus arrives and the contraction arises, at once or almost at once in different places of the ventricular masses. The first point *Q*, indicates that the stimulus arrives first at a point lying near to the apex and calls forth a contraction of moderate degree establishing a certain degree of electronegativity toward the base which is now electropositive. The direction of the point, below the horizontal portion, is due to the direction of the current through the heart and galvanometer, which is of course the reverse of the current that originates in the auricle and which gives rise to *P*. The point *R*, which immediately follows, indicates that the stimulus has arrived at the base of the ventricle calling forth a more pronounced contraction and a greater degree of electronegativity than that present at the apex. The point *S* indicates that soon thereafter, the stimulus reaches regions lying nearer to the apex of the ventricle calling forth a contraction and establishing an electronegativity which soon gains the upper hand. The horizontal portion of the electrocardiogram, between the system of points *Q*, *R*, *S*, on the one side, and the point *T*, on the other side, represents a contraction state in which the entire muscle mass of the two ventricles participates in the same measure and hence all portions are in a condition of equal negativity for which reason the string remains stationary. It is during this period that the ventricles are engaged in driving the blood out of their cavities into the aorta and pulmonic artery.

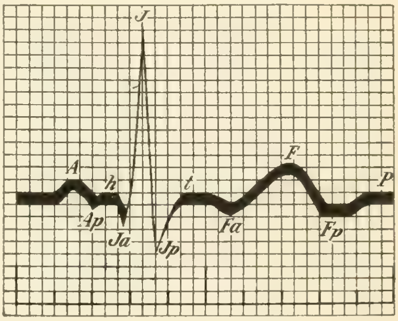


FIG. 134.—SCHEME AND INTERPRETATION OF THE ELECTROCARDIOGRAM.—(*Nicolai.*)

T, the last peak of the ventricular portion of the electrocardiogram, is directed upward and hence reveals the fact that the base of the ventricle is, at this moment, in a condition of greater electronegativity than are portions of the heart lying nearer the apex. The origin of the *T* peak has been a subject of much discussion but the investigations of Gotch have made it apparent that it is due to the contraction of muscle-fibers which have not before been brought into action, that is, fibers near the root of the aorta, in that portion of the ventricle which is the homologue of the bulbus arteriosus in the lower animals. The contraction of this region completes the discharge of the blood from the ventricular cavity.

The electrocardiogram has been further analyzed and elaborated by Kraus and Nicolai. The results of their investigations are embodied in Fig. 134. A somewhat different terminology for the different features of the general record has been introduced. Thus in this scheme the letters *A*, *Ja*, *J*, *Jp*, and *F*, replace the letters *P*, *Q*, *R*, *S*, *T*, of the Einthoven scheme.

A, expresses auricular activity, *J*[1] and *F* express respectively the *initial* and *final* activity of the ventricle. The letters *Ap* indicate a negative wave following auricular activity; *h*, represents the time during which the excitation process is passing through the auriculo-ventricular bundle (bundle of His) from its origin to its terminations. *J* designates a wave which initiates the ventricular contraction and is the result of the contraction of the system of papillary muscles. It is preceded and followed by negative waves *Ja* and *Jp*. The horizontal portion of the record, *t*, represents the contraction of the middle layers of the muscle fibers of the ventricle. *F* represents the contraction of the muscle fibers in the region of the conus arteriosus; and is likewise preceded and followed by negative waves *Fa*, and *Fp*. *P* represents the pause in the heart activities.

The activities of the different parts of the heart indicated by the lettering may be summarized as follows: (Ott.)

	Phase of Electrocardiogram.		Approximately.
A.	Activity of auricle	presystole.	Period of filling of the heart (ventricle).
h.	" " His' bundle		
J.	" " papillary system—intersystole.		Period of distention of the heart.
t.	" " middle layer of ventricular muscle	systole.	Period of ventricular discharge.
F.	" " conus arteriosus		
P.	Rest of the whole heart—pause of heart.		Period of filling of the heart.

In pathologic conditions of the heart muscle there are many deviations from the normal electrocardiogram which are more or less characteristic and of diagnostic value and importance.

THE BLOOD-SUPPLY TO THE HEART

The nutrition of the heart, its irritability and contractility, the force and frequency of the beat, are dependent on and maintained by the introduction of arterialized blood into and the removal of waste products from its tissue.

In frogs and allied animals the heart muscle is nourished by the blood flowing through its cavities. During the diastole the blood, under the influence of the slight pressure developed, passes from the interior of the heart into a system of irregular passage-ways or channels, which penetrate the heart-wall in all directions and thus comes into direct contact with the heart-cells. With the beginning of the systole the blood is forced out of these channels into the interior of the ventricle, bringing with it the products of tissue metabolism.

In mammals the entire inner surface of the heart, as shown by the investigations of Pratt, also presents a series of openings, the foramina of Thebesius, which lead into a similar series of passage-ways penetrating in various directions the heart-walls, and there are reasons for believing that the heart of the mammal may be to some extent nourished in a manner similar to the manner by which the frog heart is nourished. Thus, if a glass tube be inserted and fastened into the aortic opening of the excised heart of a cat and the interior of the ventricle filled with warm defibrinated blood of the same animal, under a pressure of about 75 mm., the heart will recommence and continue to beat for a period varying from one to several hours, thus showing that the mammalian heart may to some extent so receive nutritive material. By reason of the fact that the metabolism of the heart of the mammal is so much more active than that of the heart of the frog, this method is far from being sufficient for nutritive purposes and hence a more perfect and active blood-supply is necessitated for furnishing nutritive material and the removal of the waste products. These results are accomplished by the coronary arteries, on the one hand, and the coronary veins, on the other.

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[1] *J* has the significance here of *I*.

The Coronary Vessels.—The coronary arteries, two in number, the right and left, arise from the aorta in the pouches of Valsalva just above the right and left semilunar valves. Turning in opposite directions, they form a circle around the base of the ventricles and ultimately anastomose. From both the right and left artery branches are given off which run over the walls of both auricles and ventricles, the most important of which in man are the anterior and posterior inter-ventricular. These main vessels lie in grooves on the surface of the heart *beneath* the visceral pericardium, surrounded by connective tissue and fat. From their relation to the outer surface of the heart they may be designated *extra-mural* vessels. From these vessels small branches are given off which penetrate the walls of the heart, in which they divide into many branches and because of their relation to the heart-muscle they may be designated *intra-mural* vessels. These vessels are spoken of as *terminal arteries* in the sense that "the resistance in the anastomosing branches is greater than the blood pressure in the arteries leading to those branches" (Pratt). From these small arteries arise a rich network of capillary blood-vessels which closely invest the individual muscle cells, and which permit here a rapid and extensive interchange of nutritive and waste materials. The coronary veins arise from the union of the small veins which emerge from the capillary areas. The veins follow the course of the arteries and finally terminate in the coronary sinus, located in the auriculo-ventricular groove on the posterior surface of the heart. This sinus opens into the right auricle between the opening of the inferior vena cava and the auriculo-ventricular opening. Its orifice is guarded by a valve, which is usually single, though sometimes double.

While by far the larger portion of the blood is returned by the coronary veins, it is also certain that some of it is returned by small veins which open into little pits or depressions on the inner surface of the heart-walls, known as the foramina Thebesii. It has, however, been shown by Pratt that these foramina are present not only in the auricular walls, as generally stated, but in the walls of the ventricular cavities as well. They communicate through a capillary plexus with both arteries and veins, and by special large passages with the veins alone.

The Filling of the Coronary Arteries.—The period of time in the cardiac cycle during which the coronary (the extra-mural) arteries are filled with blood, whether during the systole or the diastole, has been a subject of much discussion. Thus it was asserted and maintained by Brücke that this event must occur during the diastole, because of the supposed fact that the semilunar valves during the systole are so closely pressed against the walls of the aorta and over the openings of the coronary arteries as to prevent the entrance of blood into them; but with the diastole and the return of the valves to their former position the blood under the recoil of the walls of the aorta would flow freely into them as well as into and through the intra-mural arteries, capillaries and veins. According to Brücke the partial emptying of the coronary arteries and their intra-mural branches, and the consequent fall of pressure within them toward the end of the diastole facilitates the systole of the ventricles, while the filling of the vessels and the consequent rise of pressure promotes the diastole. This anatomic mechanism and its associated functional activity constituted according to Brücke an apparatus by which the activity of the heart could be self-regulated. This view as to the time of the filling of the extra-mural coronary arteries has, however, been disproved.

At the present time it is generally believed as the result of many forms of experimentation that the extra-mural coronary arteries are filled during the time of the systole. For it has been shown that the semilunar valves do not close the openings of the coronary arteries by reason of the presence of blood behind them under a high pressure; that a division of one of the branches of these arteries is followed by a spurt of blood synchronous with the systole. Moreover, if a kymographic trace of the pressure within the coronary artery be compared with the trace of the pressure within the carotid artery, it will be found that there is a complete agreement between them as the pressures in the two vessels rise and fall simultaneously and as a corollary are filled during the systole. Because of the pressure which the heart-muscle must exert upon the smaller arteries and veins within its own substance during systole, it is probable that there is a temporary retardation of the flow of the blood during the systole in the coronary (the extra-mural) vessels, followed by a return of the velocity during the period of diastolic repose.

During the diastole the blood flows freely from the extra-mural vessels into the intra-mural arteries and capillaries. It is at this time too that the heart-muscle receives from the capillary blood-vessels its nutritive material and returns to the blood the products of its metabolism. During the systole the intra-mural capillaries and veins are compressed and the blood driven into the extra-mural veins. The greater the force and frequency of the beat, the larger the volume of blood passing through the coronary system.

Vaso-motor Fibers for the Coronary Arteries.—The presence in the vagus and sympathetic nerves, of vaso-motor fibers for the coronary arteries has been a subject of much investigation and discussion. By reason of the fact that stimulation of these nerves modifies the rate and the force of the heart-beat, and these in turn modify the flow of blood through the vessels, it is difficult to state whether the observed effects are the result of changes in the caliber of the arteries or to a change in the character of the heart-beat. Moreover owing to the anatomic relation which the arteries bear to the heart muscle, the rapidity of the flow through them must vary with each contraction and relaxation and thereby the difficulty of interpretation is increased. The results of direct experimental investigations of Porter, however, lead to the conclusion that the existence of vaso-motor (constrictor) fibers for the coronary arteries is highly probable.

These investigations have been corroborated by the investigations of Barbour and Prince who have found that when isolated monkey hearts are perfused with autogenous hirudin blood diluted with Locke's solution containing minute doses of epinephrin, the coronary flow is decreased. From previous experiments on rings of the coronary artery of the human heart the conclusion is drawn, that in man and the monkey, epinephrin constricts the coronary arteries even though it dilates them in the dog, cat, rabbit, and other animals. From these result the further conclusion is drawn that in man and monkeys the coronary arteries are supplied with vaso-constrictor nerves of true sympathetic (thoracico-lumbar) origin.

The Effects of Ligation of the Coronary Arteries.—As stated in a foregoing paragraph the nutrition of the heart-muscle, its irritability and contractility, depend on the blood-supply derived from the coronary vessels. This is shown by the effects which follow its withdrawal. Ligation of both coronary arteries in the dog is followed by a diminution in the force and frequency of the heart-beat, and in a few minutes by complete cessation. Ligation of even a single branch of a coronary artery of the dog heart, provided it supply a sufficiently large territory—*e.g.*, the arteria circumflexa—is sufficient to cause arrest in at least 80 per cent. of animals (Porter). With the ligation of this vessel there occurs a gradual diminution in the force and frequency of the systole. As the power of coördinate contraction declines the heart-muscle frequently exhibits a series of independent contractions of individual fibers and cells known as *fibrillary contraction.* All the results which follow ligation are to be attributed in the light of experiment to the sudden anemia which is thus established. The removal of the ligature and the return of the blood will restore the nutrition and re-establish coördinate contractions. The excised heart of the mammal which has passed into the condition of fibrillary contraction may be again made to beat rhythmically and vigorously by first cooling it with normal saline, and then perfusing it with warm defibrinated blood through the coronary vessels under a suitable pressure. The same result can be brought about by first perfusing it with a 1 per cent. solution of potassium chlorid until the heart comes to rest and then perfusing it with Ringer's solution.

The Beat of the Excised Heart.—The beat of the heart, its frequency and regularity, its continuance from the early stages of fetal development till death, has long been an interesting subject for physiologic investigation. Though related to the functional activities of the body at large, the activity of the heart is in a sense independent of them, for it will continue for a variable length of time after they have ceased. The heart of the frog or the turtle will continue to beat under appropriate conditions for hours after separation of all anatomic connections and removal from the body. The heart of the dog or cat will, however, beat but for a few minutes. The human heart would in all probability act in the same way. Nevertheless there are good reasons for believing that though the heart has ceased to respond to its customary stimulus, the irritability yet endures though perhaps in lessened degree, by reason of the absence of blood, in the mammalian heart, in the coronary system of vessels. For if, after the heart has ceased to beat for some time, warm defibrinated and oxygenated blood or Locke's modification of Ringer's solution be passed through the coronary vessels the beat will reappear and continue at its usual rate for some hours. (See paragraph relating to the action of inorganic salts on the mammalian heart, page 307.)

The reason for the longer continuance of the beat of the excised heart of the cold-blooded animal beyond that of the warm-blooded animal lies probably in the difference in the rate of their respective metabolisms. There is reason to believe that each cell of the heart-muscle, in common with other tissue cells, during life stores up and holds in reserve a larger quantity of nutritive material than is necessary for its immediate needs. When separated from the general blood-supply, the cells begin to utilize this reserved material. With its consumption the irritability declines and after a variable period of time the contraction ceases. As the metabolism is far more rapid in the warm-blooded than in the cold-blooded animal, it is probable that the reserved nutritive material is utilized more quickly in the former than in the latter other conditions being equal. So long as it lasts in either class, the irritability and contractility persist.

Whatever the immediate or exciting cause of the heart contraction may be, the fundamental condition for its manifestation is the maintenance of the irritability. So long as this persists at a sufficiently high level the heart-muscle will contract in response to the appropriate stimulus.

THE PHYSIOLOGIC PROPERTIES OF THE HEART-MUSCLE

The physiologic properties of the heart-muscle on which its efficiency as a pumping organ depends, viz., irritability, conductivity, rhythmicity, tonicity, automaticity, have been largely determined by a study of the heart of the frog. As some of the facts to be stated in subsequent paragraphs have reference to this heart, it will be found conducive to clearness if its anatomic structure and physiologic action be understood. For this reason a brief account of the frog heart will be found in the appendix.

1. **Irritability.**—The heart-muscle in common with other muscles possesses irritability, by virtue of which it responds by a change of form to the action of a stimulus. Whatever the stimulus, here, as elsewhere, there is a conversion of potential into kinetic energy—heat, electricity, and mechanic motion. The normal physiologic stimulus has not been positively determined. In common with other forms of muscle-tissue, the heart-muscle may be made to contract by artificial stimuli—*e.g.*, mechanic, thermic, chemic, and electric.

   For the demonstration of this fact it is necessary to eliminate the action of the physiologic stimulus and to bring the heart to rest in the condition of diastole. This can be done with the frog's heart, by ligating the tissues at the sino-auricular junction, a procedure which prevents the passage of the contraction wave, which originates in the sinus, over the auricles and ventricles (a fact that will be more fully alluded to in a subsequent paragraph). With the heart thus prepared and while still *in situ*, the apex may be connected with a recording lever and its evoked contractions registered on a recording surface. In this condition it will respond by a contraction to any form of an adequate stimulus, such as the induced electric current.

   In its irritability, contractility, and manner of response to stimuli, the heart of the mammal corresponds in all essential respects to the heart of the frog or turtle.

   The irritability of the heart-muscle depends primarily on the blood-supply and secondarily on the maintenance of a normal temperature, and so long as both conditions are maintained the muscle will respond by a contraction to any adequate stimulus, physiologic or artificial.

a. The Blood-supply.—The supply of blood to the mammalian heart is derived from the coronary arteries which, though filled during the systole, deliver the blood to the intra-mural arterioles and capillaries during the diastole. The facts relating to the blood-supply have been presented fully in a foregoing paragraph (page 294).

b. The Influence of Temperature.—For the manifestation of the irritability and contractility it is essential that the heart-muscle be kept at a sufficiently high temperature in order that the physiologic or a given artificial stimulus may evoke a maximal contraction. This is accomplished by immersing the suspended heart in a bath of Ringer's solution the temperature of which can be readily decreased or increased by appropriate means. The optimum temperature for the frog heart is about 25°C. As the temperature is lowered both rate and force decrease until at about from 4°C. to 0°C. both cease. Beyond 35°C. it also ceases to contract, because of a coagulation of the muscle substance. The mammalian heart attains its maximum activity at a temperature of 39°C. to 41°C. It ceases to beat at about 47°C. on the one hand and at about 17°C. on the other hand.

2. **Conductivity.**—Conductivity of living material may be defined as the ability to transmit through itself a condition of activity due to the action of a stimulus. In muscle material the condition of activity is characterized by a molecular process known as the excitation process, followed almost immediately by a change of shape known as the contraction wave.

In skeletal muscle conductivity is developed to a high degree. Thus if a stimulus, *e.g.*, an induced electric current, be sent transversely through one end of a muscle an excitation process is developed, followed by a contraction wave, both of which are conducted through the muscle without interruption to the other end with a speed, in the frog muscle, of about 10 meters per second. In the cardiac muscle the physiologic stimulus acts at or near the terminations of the venæ cavæ, from which point an excitation process and a subsequent contraction wave are conducted over the auricles, thence to the ventricles from base to apex with extreme rapidity. It is evident therefore that the heart-muscle also possesses conductivity to a high degree. It is now generally believed that the propagation of both processes is accomplished by muscle-tissue alone, independently of the nerve system. The conductivity, however, is not equally well developed in every part of the heart.

In the *frog* heart this is especially true of the tissue at both the sino-auricular and the auriculo-ventricular junctions. At these points the contraction wave is delayed for an appreciable period (a condition attributed to the embryonic character of the muscle-tissue), so that what would otherwise be a single wave becomes divided into three smaller waves, so that it becomes possible to observe and distinguish the contraction of the different chambers of the heart. In the frog's heart the excitation process and the contraction wave begin in the sinus venosus, from which they are conducted to the auricles, thence to the ventricles. The successive contractions of the walls of the subdivisions of the heart can be readily recorded with suitable apparatus. In Fig. 135, which is a graphic record of the heart-beat, the two elevations of the lever on the up-stroke, *a* and *b*, represent the contraction of the sinus and the auricle respectively, followed by the vigorous and long continued contraction of the ventricle, while the two depressions, *c* and *d*, indicate the delay in the transmission of the contraction wave at the two junctions. There is here an anatomic obstacle to the conduction of the contraction wave. The block between the sinus and the auricle may be artificially increased to such an extent as to prevent absolutely the passage of the contraction wave by ligation of the tissue between them, a procedure introduced by Stannius and now known as the first Stannius ligature. Under such circumstances the auricles and ventricle remain at rest while the sinus continues to beat at its usual rate. The obstacle between the auricles and ventricle may be increased by the same method also introduced by Stannius, and now known as the second Stannius ligature, or better by means of a suitable and adjustable clamp. By carefully regulating the pressure of the clamp it is possible to so block the wave that three or four auricular contractions may occur before the excitation process forces the block and excites a ventricular contraction. (Fig. 136.) If the block is complete, rather than partial, the ventricle will come to rest and so remain. From the foregoing facts it is evident that the physiologic stimulus exerts its action in the sinus venosus and that the auricular and ventricular beats are in turn dependent on it.

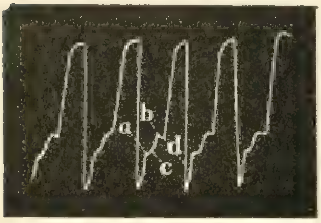

FIG. 135.—RECORD OF THE CONTRACTION OF THE FROG'S HEART.

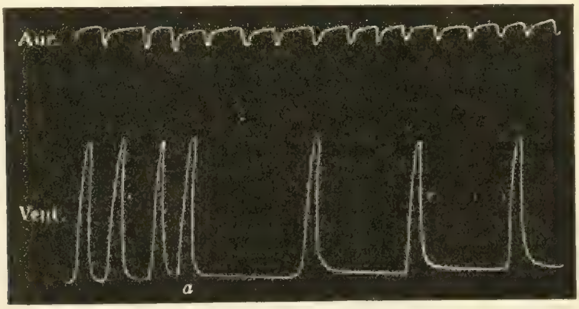

FIG. 136.—RECORD OF THE AURICULAR AND VENTRICULAR CONTRACTIONS BEFORE AND AFTER THE CLOSURE OF THE CLAMP AT *a*.

In the *mammalian* heart the seat of the stimulus and the point of origin of the excitation process and the subsequent contraction wave have been a subject of much investigation and discussion. For some time it has been believed that these processes originate at the terminations of, or between the terminations of the venæ cavæ in a region corresponding to the sinus venosus in the frog heart[1], from which they pass over the auricles, thence to the ventricles. On the basis of this belief it has been assumed that there is a specialized area in which the stimulus arises and which determines the rate and rhythm of the entire heart. At present it is believed that this area is identical with the region occupied by the sino-auricular node, the lower portion of the sulcus terminalis. With the view of determining the truth of this assumption Flack performed a number of experiments on the hearts of dogs, cats, and rabbits, some of the results of which, abstracted from his paper, are as follows: The application of cold either through metallic tubes or by means of an ethyl chlorid spray, the remainder of the heart being protected, caused slowing of both auricles and ventricles. Weak electric stimulation caused marked inhibition of both auricles and ventricles; slightly stronger stimulation caused a mixed effect of inhibition and acceleration, the latter usually predominating; still stronger stimulation gave rise to marked acceleration of the whole heart rhythm or an altered rhythm of auricles and ventricles. When electric stimuli were applied to other regions of the superior vena cava or sulcus no effects were noticeable.

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[1] In the mammalian heart the sinus venosus as a distinct chamber has been obliterated, but it is represented by the following remnants: (1) The termination of the superior vena

Mechanic stimulation as pinching the node with forceps called forth similar results. Destruction of the node, however, had no effect on the rhythm. The application of a weak solution of atropin abolishes the customary effects of both vagus and sympathetic nerve stimulation. From the foregoing facts it may be assumed that the usual seat of origin of the stimulus to the cardiac contraction is the sino-auricular node, but as the heart continues to contract after the node is destroyed, it is evident that some other portion or portions of the auricular wall are also capable of developing under the circumstances an adequate stimulus.

A further proof that the sino-auricular node is the initiator of the cardiac contraction is found in its change of electric potential. It has long been established that when any portion of living material enters into a state of activity it becomes electro-negative to all other portions which are at the same instant electro-positive. Lewis with special electrodes in connection with a string galvanometer found in a series of determinations that with the beginning of a cardiac contraction, the sino-auricular node was the point of initial electro-negativity, a fact that is in accord with the general truth that the region of greatest activity exhibits the greatest degree of negativity. The sino-auricular node may therefore be regarded as the primary seat of the stimulus or excitation process and the initiator of the beat.

From the sino-auricular node the excitation process is conducted to the auricles and ventricles in quick succession, though between the end of the auricular contraction and the beginning of the ventricular contraction there is also a perceptible interval similar to that observed in the frog heart. For a long time it was assumed that the excitation process and the contraction wave passed directly from auricles to ventricles across the auriculo-ventricular junction as in the frog and that the interval

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cava (the right duct of Cuvier); (2) the coronary sinus (the left duct of Cuvier); (3), a stratum submerged beneath auricular tissue at the tænia terminalis; (4) the remnants of the venous valves, *i.e.*, the Thebesian and Eustachian valves (Flack). In addition there is a remnant of primitive tissue at the sino-auricular junction, that is, where the superior vena cava joins the tænia terminalis of the right auricle, and known as the sino-auricular node.

between the auricular and ventricular contractions was due to an interference with the passage of the contraction wave across the junction because of the extreme scarcity of the muscle fibers in this region or to their embryonic character. In recent years, however, this view has been abandoned because the real bond of union between the auricular and ventricular tissues, across which the excitation process passes, has been found, as stated on page 271, in the system of muscle-fibers, described in part by His, Retzer and Bräunig, and Tawara and in part by Keith and Flack and known as the *conduction system of the heart*, page 272. This system it is believed constitutes the anatomic and physiologic path across which the excitation process passes from auricles to ventricles. The excitation process originating in the sino-auricular node passes first to the auricular walls, exciting them to contraction and then into and through the auriculo-ventricular bundle to the ventricular walls, exciting them to contraction. The supposition that this was the case has been demonstrated by Hering and others who succeeded in dividing the muscle-bundle in the excised hearts of rabbits and dogs, kept actively beating by perfusion with Ringers' solution. On division of the bundle both auricles and ventricles continued to beat though with different rates and independently of each other. These and other experiments of a similar character have demonstrated beyond question that the auriculo-ventricular bundle with its widespread ramifications is the true conducting system between auricles and ventricles. In this system the sino-auricular node is regarded as the primary dominating "pace maker" of the rate and rhythm of the heart. Inasmuch, however, as the heart will continue to beat, after the destruction of the sino-auricular node it is evident that it is not the only region that can initiate the contraction. Whether the contraction under such circumstances is due to an excitation arising in some other portion of the auricular wall or in the subsidiary auriculo-ventricular node is a subject of discussion. The cause assigned by Tawara, for the interval between the auricular and ventricular contraction is not so much the embryonic character of the fibers of the system, as it is the length of the system as a whole, which he estimates at from 4 to 6 centimeters. This time, estimated from the beginning of the auricular systole to the beginning of the ventricular systole amounts to from 0.1 to 0.2 second. The interval between these two events, determined from the time between the occurrence of the *a* and the *c* or *s* waves on the jugular pulse tracing is known as the *a-c interval*, or the *As-Vs interval.*

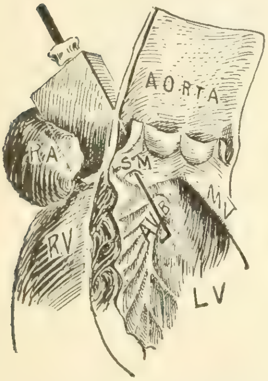

FIG. 137.—The Erlanger heart-block clamp compressing the auriculo-ventricular bundle (AVB). SM, Septum membranaceum; MV, mitral valve.—(*Hirschfelder.*)

With the mammalian heart as with the frog heart it is possible to increase the length of the interval between the auricular and the ventricular contraction, the inter-systolic period, by compression of a portion of the tissues between auricles and ventricles including presumably the central part of the conducting system, the muscle bundle of His. This has been accomplished in the dog by Erlanger by means of a specially devised hook clamp (Fig. 137), which consists of an L-shaped hook of steel wire the arm of which can be made to approach a brass block by means of a bolt and screw. The L-shaped hook is inserted into the right wall of the aorta, then passed downward and backward into the left ventricle, then pushed through the ventricular septum into the right ventricle. In this position it lies under the auriculo-ventricular bundle. Compression is now brought about by approximating the hook to the brass block by means of the nut. When the compression is brought about suddenly and completely the ventricles at once cease beating, though the auricles continue to beat with their customary rate and regularity. After a variable period of time, varying from a few seconds to 70 seconds, during which the ventricles are relaxed and gradually filling with blood from the auricles, the ventricular beat returns, at first slowly but with a gradually increasing frequency until a definite but a comparatively slow rate is attained. The rhythm thus developed is termed the *ideo-ventricular* rhythm.

In experiments on the dog heart performed by Erlanger the following results were obtained when the auriculo-ventricular bundle was completely crushed.

Aur. rate per minute.	Ven. rate per minute.	Ratio of Aur. to Ven.
Max. 216	Max. 69.8	3.09
Min. 117.8	Min. 34.8	3.38
Ave. 166.9	Ave. 52.3	3.19

The reason assigned for the cessation of the ventricular contraction is the non-arrival of the excitation process at the ventricular end of the conducting system, because of the blocking or compression. Under physiologic conditions the ventricular beat is directly dependent on the arrival of the excitation process from the auricles and if it fails to arrive the ventricle does not contract for some seconds. The return of the beat during complete blocking is attributed to the development of a hitherto dormant inherent rhythmicity. When this is established both auricles and ventricles continue to beat though with totally different rhythms.

The effects which follow gradual compression of the muscle-bundle are somewhat different from those which follow sudden compression. If the clamp is accurately adjusted and the compression gradually applied, the first perceptible effect is a lengthening of the normal pause, the inter-systolic, between the auricular and the ventricular contraction. With an increase in the compression there will come a moment when one of the auricular contraction waves fails to reach the ventricle, or if it does, it is so enfeebled that it is incapable of exciting the ventricle, which in consequence fails to contract. This dropping out of a ventricular contraction may occur once in every 10, 9, 8, 7, 6, etc., auricular beats, in accordance with the degree of compression. With a further tightening of the clamp, the blocking of the excitation process may be still further increased so that only every second, third, or fourth auricular beat is capable of developing a ventricular beat, establishing what has been termed the 2 : 1, 3 : 1, 4 : 1, rhythms respectively; and finally when the blocking is complete no excitation process can reach the ventricle.

Owing to the capability of the mammalian ventricle to develop an independent rhythm when not stimulated by the auricles for a few seconds or more, it is not always possible to state at what particular moment in the successive stages of compression the independent ventricular rhythm becomes manifest. Usually when the rhythm is of the 3 : 1 type, *i.e.*, when the third auricular contraction fails to reach the ventricle, it will begin to beat of itself. Under such circumstances the auricles and ventricles become dissociated even though the block is not quite complete.

These experimental facts have afforded an explanation of the altered rhythm between auricles and ventricles often found in that pathologic condition known as Adams-Stokes disease. In this disease the rhythm may be any one of the rhythms stated in the foregoing paragraph. In two instances the following ratio of the ventricle to the auricle was observed by Erlanger.

Aur. rate per minute.	Ven. rate per minute.	Ratio of Aur. to Ven.
79.6	22.4	3.55
84.6	31.0	2.73

In a few cases of death from this disease a post-mortem examination showed a lesion of the auriculo-ventricular bundle.

3. **Rhythmicity.**—Rhythmicity may be defined as the ability to act in regularly recurring cycles or the property of anything so acting. As the heart-beat recurs in regular cycles or at regular intervals, it may therefore be said that the heart-muscle is characterized by rhythmicity. The beat of the heart as well as each phase of the beat occupies a regular measure of time and is therefore rhythmic in character. Experimental procedures, however, show that the rhythmic power or at least the frequency of the rhythm varies in each of its subdivisions when they are separated one from the other. Thus if the tissue between the sinus and auricle in the frog or turtle heart be divided, the auriculo-ventricular portion at once ceases to beat, while the sinus continues to beat as usual. In a short time, however, the auricles and ventricles begin again to beat, but with a slower rhythm. Division of the tissue between auricles and ventricles is again followed by rest. In a short time the auricles begin to beat, while the ventricle remains quiescent. If the ventricle now be stimulated in a rhythmic manner it may resume rhythmic activity. These facts are taken as an indication that the rhythmic power is greatest in the sinus, less in the auricles, and least in the ventricles.

In the warm-blooded animal, *e.g.*, dog, cat, rabbit, there is also a difference in the rhythmicity of the auricles and ventricles. This is shown by the effects which follow division of the auriculo-ventricular bundle, or sudden and complete compression of that portion of the auriculo-ventricular tissue containing it. In either case the ventricle for a short time remains at rest, though the auricles continue to beat at their usual rate. After a variable number of seconds the ventricle develops a rhythm of its own, though it never attains that of the auricle. From these facts it is probable that in each division of the heart a stimulus similar to that acting in the sinus is developed when the heart chambers are separated one from the other.

4. **Tonicity.**—Tonicity may be defined as a condition of muscle material characterized by a slight degree of contraction which varies in extent, however, from time to time under physiologic conditions. Whatever the cause of the tonicity may be in any given form of muscle, the slight degree of contraction which characterizes it not only resists undue extension but permits of a quicker response to the action of a stimulus and a more effective performance of work. The heart-muscle, like the skeletal muscle, maintains continuously a certain degree of contraction, which not only prevents undue expansion of the heart during the period of diastole, but increases its efficiency as a pumping organ at the beginning and during the systole. The results obtained from subjecting the heart muscle to the action of a calcium salt renders it probable that the tonicity is in large measure the result of or is associated with the action of such a salt (see page 306). The tonicity may, however, be increased or decreased by the action of various external agents. Thus the passage of dilute solutions of various drugs—*e.g.*, alkalies, digitalis—through the cavities of the excised heart will so increase the tonicity, or the contractile power, that complete relaxation is prevented, until finally the heart comes to a standstill in the condition of systole. The passage of dilute solutions of lactic acid, muscarine, etc., through the heart will, on the contrary, so decrease the tonicity or the contractile power that the normal contraction is not attained. The relaxation therefore gradually increases until the heart finally comes to a standstill in the condition of extreme diastole. In the first instance the tonicity is said to be increased; in the second instance, decreased.
5. **Automaticity.**—Automaticity may be defined as the power of maintaining activity by a self-acting cause or the power of acting independent of external causes. Inasmuch as the heart continues to contract in a perfectly rhythmic manner after removal from the body and apparently without the aid of an external stimulus, it is said that the heart-muscle is automatic or spontaneous in action. Strictly speaking, however, this is not the case, for the reason that all movement, that of the heart included, is the resultant of the action of natural causes though their true nature may be beyond the reach of present methods of investigation.

The Nature of the Stimulus.—As the heart continues to beat after removal from the body, it is evident that the stimulus does not originate in the central nerve system but in the heart itself. Two views have been held as to its origin and nature:

1. That it originates in the nerve-cells found in various parts of the heart-muscle; that it is a nerve impulse rhythmically and automatically discharged by these cells and transmitted by their axons to the heart-muscle cells.
2. That it originates in the muscle-cells themselves; that it is chemic in character and due to a reaction between the chemic constituents, organic and inorganic, of the muscle-cells and those of the lymph by which they are surrounded.

According to the first view the stimulus is *neurogenic*, according to the second view *myogenic*.

The presence of nerve-cells; their relation to the muscle-cells; the pronounced rhythmic activity of the sinus and auricles in which the nerve-cells are abundant; the feeble activity of the apex, in which they are wanting—these and other facts lend support to the view that the stimulus originates in the nerve-cells. To them have been attributed the power of automatic activity.

The absence of nerve-cells in portions of the heart-muscle, which nevertheless exhibit rhythmic contractions for quite a long period of time; the rhythmic beat of the embryonic heart before the migration of nerve-cells to its walls shows that the stimulus does not necessarily originate in nerve-cells. Moreover, Porter has conclusively shown that the apex of the dog's heart, which is generally believed to be totally devoid of nerve-cells, can be made to beat for hours by feeding it through its nutrient artery with warm defibrinated blood. Unless it be assumed that the heart-muscle contracts automatically, without a cause, it is a fair assumption that the exciting cause of the contraction arises within the muscle-cells themselves, and that it is in all probability the outcome of a reaction between the chemic constituents of the blood or lymph on the one hand, and the chemic constituents of the muscle-cells on the other. The discovery that some of the inorganic salts of the blood have a specific physiologic action on the heart-muscle was made in 1882 by Ringer. Since then, many attempts have been made to isolate these constituents, to determine not only their individual, but also their collective action, when combined in proportions approximating those in which they exist in the blood.

The Action of Inorganic Salts.—1. *On the Frog and Terrapin Heart.*—The inorganic salts which are most directly concerned in exciting and sustaining the heart-beat are sodium chlorid, calcium phosphate or chlorid, and potassium chlorid. A combination of these salts in the proportions in which they exist in the blood was first suggested by Ringer and is made by saturating a 0.65 per cent. solution of sodium chlorid with calcium phosphate, and then adding to each 100 c.c., 2 c.c. of a 1 per cent. solution of potassium chlorid. A frog's heart immersed in this solution will continue to beat for some hours. A combination of the chlorids of sodium, calcium, and potassium in amounts which will vary for different animals is equally efficient in maintaining the heart-beat.

The collective as well as the individual actions of these salts have been strikingly brought out by the experiments of Profs. Howell and Greene, from whose published results the following statements are derived. Instead of employing the entire heart, they used for various reasons strips from the terminations of the venæ cavæ and from the ventricle of the terrapin heart. The proportion of the inorganic salts most favorable for the contraction of the vena cava strips is the following: viz., sodium chlorid, 0.7 per cent.; calcium chlorid, 0.026 per cent.; potassium chlorid, 0.03 per cent. When vena cava strips are immersed in this solution, they begin in a short time to exhibit rhythmic contractions which may continue for several days. In the same strength of solution the ventricular strips remain inactive but if the percentage of the calcium chlorid be raised from 0.026 per cent. to 0.04, or 0.05 per cent., spontaneous contractions soon develop and continue for several days or more. In the foregoing solution when the calcium chlorid is present only to the extent of 0.026 per cent., though the ventricular strip does not contract, it is kept in good condition for contraction, for even after many hours the raising of the percentage of calcium chlorid to 0.04 or 0.05 per cent. will call forth after a brief latent period, rapid and energetic contractions. From this fact it is inferred that the vena cava region is more sensitive to the combined action of the salts than is the ventricle.

The action of the individual salts is also best shown with ventricular strips. In a 0.7 per cent. sodium chlorid solution the strip beats rhythmically and energetically, but only for a short period and with gradually diminishing force, and a loss of tonicity until it entirely ceases to beat. A reason assigned for this is the removal of other salts necessary to the excitation of the contraction. In a calcium chlorid solution—0.9 per cent.—*i.e.*, isotonic with the sodium chlorid—the heart strip is thrown into strong tone, but does not rhythmically contract. If, however, the strip is placed in normal saline, and calcium chlorid added in amounts equal to that present in the blood, it will after a very short period begin to contract rapidly and energetically and for a longer time than when in sodium chlorid solution alone. The contractions not infrequently occur before relaxation is completed, so that the strip passes into the condition of contracture.

In potassium chlorid solutions isotonic—0.9 per cent.—with sodium chlorid solution the heart strip also fails to contract. This is the case also when the potassium is added to the sodium chlorid in amount practically equal to that found in the blood.

2. *On the Mammalian Heart.*—The collective action of the inorganic salts on the isolated heart of all members of this class of animals which have been made the subject of experimentation, is as marked, if not more so, than it is on the heart of the frog or terrapin especially when the coronary blood-vessels are perfused with Ringer's solution or the modification of it suggested by Locke, as follows: $NaCl$ 0.90 per cent.; $CaCl_2$ 0.024 per cent.; KCl 0.042 per cent.; $NaHCO_3$ 0.02 per cent., dextrose 0.1 per cent. The reviving and sustaining power of this solution is extraordinary. Locke and Rosenheim were able to revive the isolated heart of a rabbit and to excite it to active contraction, for several hours at a time, on four consecutive days by perfusing it with this solution saturated with oxygen and at a temperature of 35°C. No special precautions were observed other than keeping it cool (10°C.) and moist during the intervals of experimentation. The duration of the irritability and contractility extended over a period of 95 hours. Kuliabko revived the heart of a rabbit for an hour nearly three days after removal from the body of the animal. It was then placed on ice, and after four days it was again revived by perfusing it with Ringer's solution. Altogether this heart retained its irritability for seven days. Hering revived the heart of a monkey on three different occasions, the first, 4½ hours, the second, 28 hours, and the third 54 hours after the death of the animal. In the intervening periods the heart was also kept on ice. In this animal it was even possible to increase and decrease the activity of the heart by stimulation of the nerves which normally control the rate of the beat. Kuliabko was also able to revive the isolated heart of a child 20 hours after death from a double pneumonia. It was made to beat rhythmically at a rate varying from 70 to 80 per minute when the solution had a temperature of 39°C., and at a rate of

98 to 102 per minute when it had a temperature of 41°C., though at this temperature the beat became arrhythmic. All these instances demonstrate the extreme persistence of the irritability of the heart-muscle under appropriate conditions.

The action of individual salts has been shown experimentally on the hearts of rabbits, cats, dogs, monkeys, by Gross, Howell and others. Thus it has been found that when an isolated heart is rhythmically beating in response to the perfusion of Ringer's or Locke's solution, the addition of potassium chlorid in small amounts is followed by a decrease in the rate and force of the contraction, and in larger amounts by a complete cessation of the contraction and a standstill in diastole. On the withdrawal of the potassium, the former frequency and vigor are regained.

Under the same conditions, the addition of calcium chlorid in sufficient amounts is followed by an increase in the rate and in the vigor of the contractions; on its withdrawal both rate and force return to the previous condition. Potassium exerts a depressor or an inhibitor influence on the irritability and contractility of the heart-muscle. Calcium exerts an accelerator and an augmentor influence on the irritability and contractility of the heart.

A Theory of the Heart-beat.—From the foregoing facts it seems probable that the heart-beat is connected with and dependent on the presence and interaction of the inorganic salts present in the lymph, though as to the manner in which they interact to initiate the beat, there is some obscurity. A very plausible theory as to the part played by the inorganic salts in initiating the contraction and one apparantly in accordance with the facts has been presented by Howell as follows:

The heart-muscle, it is assumed, contains a stable organic energy-yielding compound of which potassium is one of the constituents and on which its stability depends. This compound must be present in relatively large amounts as the heart will continue to contract and expend energy for many hours after the blood-supply has been withdrawn.

During the diastole a reaction takes place between this compound and the calcium or the calcium and the sodium salts, whereby a portion of the organic compound is freed from potassium and is then combined with calcium or with calcium and sodium. In consequence, this portion of the organic compound in combination with the calcium acquires and gradually increases in instability, reaching its maximum at the end of the diastole, when it undergoes a dissociation giving rise to a chain of events that culminate in a contraction. The initial step, therefore, is a dissociation of a complex unstable molecule followed by an oxidation of the dissociated products. That an active dissociation of some character takes place is evident from the consumption of oxygen, the production of carbon dioxid, the liberation of heat, electricity, and mechanic motion.

Inasmuch as the contraction is always maximal and as the heart is refractory to a stimulus during the systole, the probabilities are that all of the unstable portion of the energy-yielding compound is dissociated with each contraction. With the relaxation there is a renewal of the unstable combination of calcium with the organic molecules, which increases in amount until the maximum is again attained when another dissociation occurs followed by another contraction. The rhythmicity of the heart's action, the appearance of a refractory condition during the systole and its gradual disappearance during the diastole, as well as other phenomena, are readily explained by the foregoing hypothesis.

The cause of the dissociation of the energy-yielding material is, however, a subject of discussion. According to Howell it is not necessary to assume the presence of any cause other than the extreme instability of the organic compound in question. According to Engelmann, Langendorff and others, the dissociation is not spontaneous but is the result of the action of a specific stimulus, an "inner stimulus," arising within the muscle elements themselves through metabolic processes; and so long as these processes are chemically and physically conditioned by blood or tissue fluids containing the inorganic salts, so long will this stimulus be produced. As to the nature of this stimulus, whether chemic, electric or enzymic, nothing definite can be stated at present.

The Response of the Heart to the Action of an Artificial Stimulus.—The heart of the frog as well as of some other animals may be brought to a standstill by the ligation of the tissues between the sinus venosus and the auricle, a procedure first introduced by Stannius and now known as the first Stannius ligature. Under such circumstances the heart may be made to contract by stimulating it with the single induced current. With each passage of the current the heart contracts. Contrary to what is observed in skeletal muscles, the heart contraction, if it occurs at all, at once reaches its maximal value. Any increase in the strength of the stimulus above the threshold value has no greater effect on the extent or force of the contraction than the minimal stimulus. A conclusion which may be drawn from this fact, according to Engelmann is as follows: By reason of the fact that the heart contracts at its maximal value to the action of any strength of stimulus, under given conditions, there is always ensured a more or less complete emptying of the ventricular contents and a uniform discharge of blood into the arteries, which would not be the case if the extent of the contraction varied with the strength of the stimulus; and there are reasons for believing that the normal stimulus for the contraction varies within wide limits above the threshold value both in normal and abnormal conditions of the heart. The changes in the extent or force of the contraction are the result, not of changes in the intensity of the stimulus, but of changes in the heart-muscle, caused by variations in mechanical resistances.

The periodicity of the heart's action or its rhythm may also be elucidated by the foregoing facts. There are reasons for believing that at the time of the contraction practically all of the available energy-yielding material is completely utilized, after which the heart relaxes and remains at rest in the diastolic condition for a given period; and before a second excitation wave can be developed and pass from the sinus over the heart there must be a re-accumulation of energy-yielding material, and a restoration of the irritability. This is accomplished during the diastole. By virtue of this fact the heart cannot act otherwise than in a periodic manner.

Inasmuch as there is a conversion of all of the potential energy into kinetic energy during the systole, there is of necessity, a lowering of the irritability, and to so great an extent is this the case that the heart will not respond to the action of a second stimulus either physiologic or artificial during the systolic period. This non-responsiveness of the heart may be shown by throwing into it a second stimulus at any moment during the systole. Whatever the moment or whatever the strength of the stimulus may be the extent of the contraction remains the same. During the systolic period the heart is said, therefore, to be *refractory* or non-responsive to a second stimulus. If, however, a second stimulus of average strength be thrown into the ventricle at any moment during the relaxation, a second contraction will be developed, which is known as the extra systole (Fig. 138).

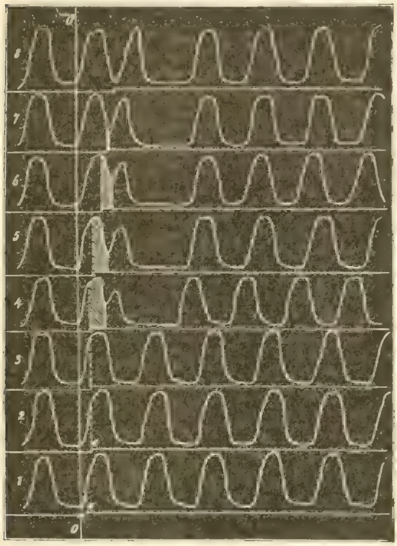

FIG. 138.—MYOGRAMS OF THE FROG'S VENTRICLE SHOWING THE EFFECTS OF AN INDUCED ELECTRIC CURRENT SENT INTO THE VENTRICLE AT DIFFERENT TIMES OF THE CYCLE.—(*Marey.*)

oo' indicates the beginning of the contraction in each series. The break in the line *e*, indicates the time the stimulus is sent in. In 1, 2, 3, the stimulus falls into the ventricle in the non-responsive period or the refractory period, *i.e.*, during the systole when the irritability has practically disappeared. From 4 to 8 the stimulus falls into the ventricle in the responsive period or the period of returning and increasing irritability, *i.e.*, at the end of the systole and during the diastole. The width of the shaded lines is a measure of the latent period, *i.e.*, the period between the time of stimulation and the beginning of the resulting contraction which diminishes as the diastole progresses.

The Extra Systole.—The extent of this extra systole will be proportional to the time at which the stimulus is thrown into the ventricle as it passes from the beginning to the end of its relaxation. Whatever the extent of the extra systole, its height is no greater than that of the first systole. For this reason it is believed a tetanic contraction cannot be developed. If the stimulus be thrown into the heart just as the relaxation is completed, the extra systole attains the same height as the preceding systole. In passing from the beginning to the end of the relaxation and into the diastolic or resting period, it has been found that the extra systole can be evoked by a stimulus which is steadily decreased in intensity. It is evident from this fact that the restoration of the energy-yielding material and the return of the irritability gradually increases from the beginning of the relaxation to the end of the diastole (Fig. 139). For this reason weak stimuli are more effective in the later than in the earlier period of the relaxation and the diastole.

After the development and disappearance of the extra systole a considerable pause in the heart's action occurs to which the term *compensatory pause* has been given on the assumption that it was necessary on the part of the heart to compensate for the disturbance of the rhythm by remaining at rest until the time of the next beat and thus restore the rhythm. This was thought to be a special property of the heart-muscle. This view, however, is no longer entertained. For if an isolated ventricle of a frog heart be employed and made to contract rhythmically by an artificial stimulus, or if a spontaneously beating portion of the dog's heart be employed for experimentation instead of the whole heart, the results of the same methods of stimulation are different. Though an extra systole is called forth as usual, there is no compensatory pause; indeed, if anything the pause is shorter than the regular pause. The theory that a compensatory pause is necessitated for the restoration of the normal rhythm is therefore not tenable.

The explanation assigned and generally accepted at present for the production of a compensatory pause is as follows: In a spontaneously beating heart the ventricular systole is evoked by the arrival of an excitation process coming from the auricles. When the extra systole is induced by an artificial stimulus, the next succeeding excitation from the auricle falls into the refractory period and hence the ventricle is not stimulated. It, therefore, simply waits for the arrival of the second succeeding excitation, when it responds and takes up the regular rhythm.

This fact is of great interest clinically for it frequently happens that extra systoles of the ventricle arise in the human heart in conditions of the circulation characterized by a high blood-pressure and especially when there is coincidently an impairment in the irritability and contractility of the heart-muscle. Extra systoles, however, may have their origin in the auricular walls as well.

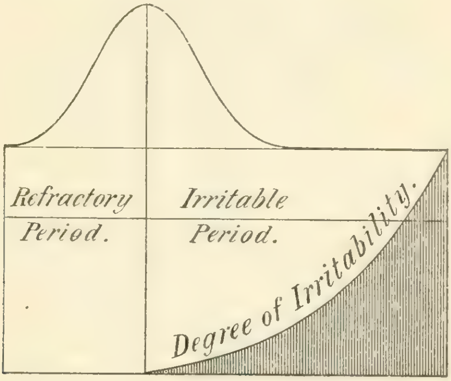

Fig. 139.—Diagram Showing the Variations of Irritability during the Systole and the Diastole.—(*Modified from Waller.*)

If a series of successive stimuli be thrown into the heart-muscle the effect will vary in accordance with their time intervals. Should this be less than about three seconds there will be a gradual increase in the height for some half dozen contractions, a result to which the term "staircase" or "*treppe*" has been given. This increase in the height of the contraction is attributed to an increase in the irritability and contractility of the muscle the result of the primary stimulating action of fatigue products.

THE NERVE MECHANISM OF THE HEART

By this term is meant a combination of nerves and nerve centers which coöperate to increase or decrease either the rate or force of the heart's contraction, and hence the proper distribution of the blood, in accordance with the activities of different organs of the body. That the heart is normally influenced by nerve centers in response to nerve impulses transmitted to them in consequence of cerebral (psychic) or physiologic activities in different parts of the body is a matter of personal experience; that the heart is abnormally influenced by the same nerve-centers in response to nerve impulses transmitted to them in consequence of pathologic and traumatic processes occurring in different regions of the body, and that both heart and nerves are modified in different ways by the action of drugs introduced into the body, are matters of daily clinical experience.

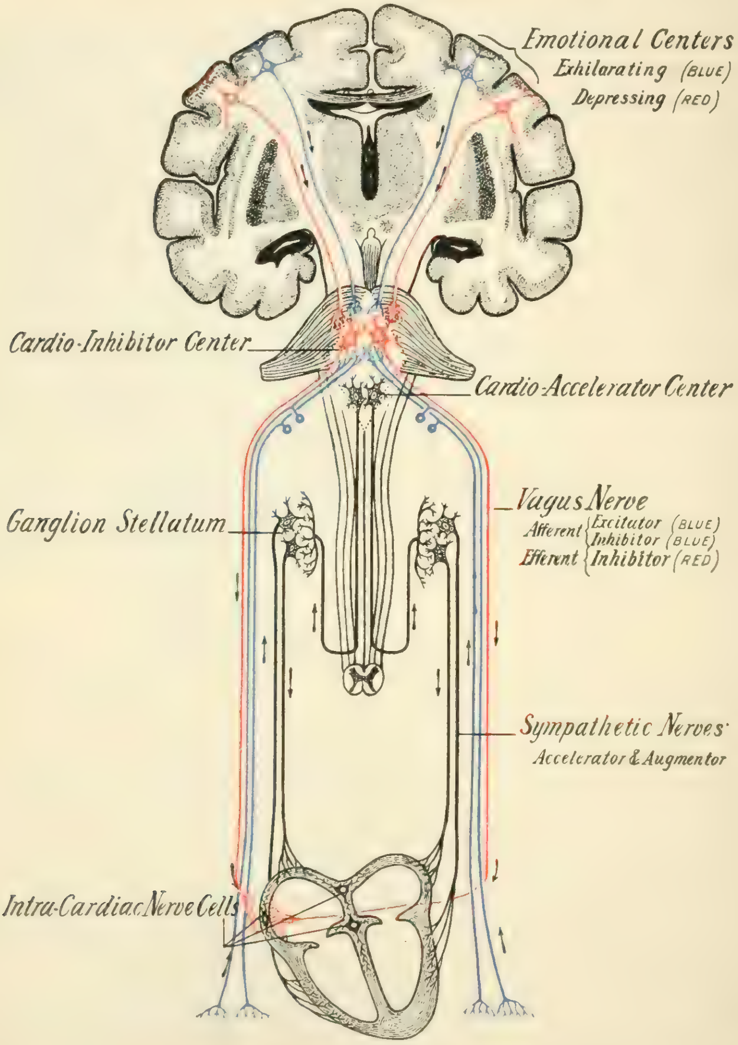
Emotional Centers
Exhilarating (BLUE)
Depressing (RED)
Cardio-Inhibitor Center
Cardio-Accelerator Center
Vagus Nerve
Afferent {Excitator (BLUE)
Inhibitor (BLUE)
Efferent {Inhibitor (RED)
Ganglion Stellatum
Sympathetic Nerves
Accelerator & Augmentor
Intra-Cardiac Nerve Cells

FIG. 140.—DIAGRAM OF THE NERVE MECHANISM OF THE HEART.—(*G. Bachman.*)

The nerves comprising this mechanism and the relation they bear one to another are represented in Fig. 140.

It was stated in a previous paragraph, page 297, that the contraction of the heart-muscle is independent of its connection with the central organs of the nerve system, and that it will continue to contract in a rhythmic manner for a variable length of time even after its removal from the body of the animal, the length of time varying with the animal and the conditions to which it is subjected; that the stimulus is myogenic and chemic in character, the result of a reaction between the chemic constituents, organic and inorganic, of the muscle-cells and those in the lymph by which they are surrounded. It has also been further shown that even in the living animal the heart will continue to beat and fulfil its functions after division of all nerves in connection with it. A dog thus experimented on lived for eleven months, and beyond the fact of becoming fatigued more readily upon exertion than formerly, exhibited no striking disturbance of its functions. Nevertheless groups of nerve-cells are present in certain portions of the heart in all classes of vertebrate animals, which bear an anatomic and physiologic relation to the heart-cells on the one hand, and to the nerves connecting them with the central organs of the nerve system on the other hand.

Intra-cardiac Nerve-cells.—In the frog heart a group of nerve-cells is found in the sinus at its junction with the auricle, known as the crescent or ganglion of Remak; a second group is found at the base of the ventricle on its anterior aspect, and known as the ganglion of Bidder; a third group is found in the auricular septum, known as the septal ganglion, or the ganglion of v. Bezold or of Ludwig. The majority of the cells are situated on the surface of the heart just beneath the pericardium. From the cell-body fine non-medullated fibers pass into the substance of the heart, to become histologically and physiologically related with the muscle-fiber.

In the dog heart and in the mammalian heart generally, though nerve-cells are present, they are not arranged in such definite groups, but are more widely distributed in the terminations of the venæ cavæ, pulmonary veins, the walls of the auricles, and in the neighborhood of the base of the ventricles.

Extra-cardiac Nerves.—The extra-cardiac nerves which connect the heart with the central nerve system and through which the activities of the heart are influenced are two: viz., the sympathetic and the vagus or pneumogastric. Experimental investigation has established the fact that the sympathetic is the motor nerve to the heart, the nerve which accelerates the rate and augments the force of the normal beat; while the vagus is the inhibitor nerve, the nerve which inhibits or controls the rate and the force of the beat in accordance with the necessities of blood distribution. For this reason these two nerves will be considered in the order stated. The course of the fibers composing these nerves, from their origin to their termination, and the relation they bear to one another and to neighboring structures, vary somewhat in different animals.

The Origin and Distribution of the Sympathetic Nerves in Mammals.—The sympathetic nerve-fibers which influence the action of the heart, are connected on the one hand with the heart-muscle itself and on the other hand with nerve-fibers coming from the central nerve system. The former are non-medullated and post-ganglionic, the latter medullated and pre-ganglionic.

The pre-ganglionic fibers have their origin in the medulla oblongata and very probably from nerve-cells in the gray matter beneath the floor of the fourth ventricle. From this origin they descend the spinal cord as far as the level of the second, third, and at times the fourth thoracic nerves. At this level they emerge from the cord in company with the nerve-fibers composing the anterior roots of the second third, and fourth thoracic nerves. After a short course, they enter the white rami communicantes, then the sympathetic chain and pass upward to the ganglion stellatum (the first thoracic), and by way of the annulus of Vieussens (in the dog) to the inferior cervical ganglion as well, around the nerve-cells of both of which their terminal branches arborize.[1] From the nerve-cells of both the stellate and inferior cervical ganglia, the sympathetic nerves proper arise, which after emerging from the ganglia pass toward the heart and become associated with the fibers of the vagus and assist in the formation of the cardiac plexuses. On reaching the heart they may terminate directly in the muscle-cell or indirectly through the intermediation of intra-cardiac nerve-cells. The former mode of termination is the more probable. Experiment has shown that both the pre- and post-ganglionic fibers are efferent in function.

The Origin and Distribution of the Vagus Nerve in Mammals.—The vagus nerve-fibers which influence the heart are connected on the one hand with the heart, through the intermediation of the intra-cardiac cells, and on the other hand with the central nerve system. Histologic investigation has shown that the vagus nerve-trunk of man and mammals generally, contains medullated fibers of large and small size. Experiment has shown that the large fibers are *afferent*, the small fibers *efferent* in function.

The large afferent fibers arise in the ganglia situated on the trunk of the nerve. From their contained nerve-cells a short axon process proceeds which soon divides into a central and a peripheral branch. The central branch passes toward and into the gray matter beneath the floor of the fourth ventricle, where its end-tufts arborize around nerve-cells; the peripheral branch passes toward the general periphery to be distributed to the mucous membrane of the lungs, stomach, intestine, etc.

The small efferent fibers are the peripherally coursing axons of nerve-cells situated in the gray matter beneath the floor of the fourth ventricle at the tip of the calamus scriptorius. The exact course of these fibers from their origin into the trunk of the vagus is not positively known. According to some investigators, they leave the medulla by way of the spinal accessory nerve and enter the trunk of the vagus through its internal or anastomotic branch; according to recent investigations made by Schaternikoff and Friedenthal, they leave the medulla along the path by which the afferent fibers enter and never become associated with the spinal accessory nerve at its origin.

In the neighborhood of the inferior or recurrent laryngeal nerves, branches containing efferent fibers are given off, which pass to the heart by way of the cardiac plexus. The terminal branches of these fibers are not distributed directly to the heart-muscle, but to the intra-cardiac nerve-cells, around the bodies of which they end in basket-like formations. The fibers in the vagus are pre-ganglionic; those of the nerve-cells post-ganglionic. (See Fig. 140.)

The Origin and Distribution of the Sympathetic and Vagus Nerves in the Frog.—In the *frog* and allied animals the relation of these two sets of nerve-fibers, viz., the efferent sympathetic fibers and the efferent vagus fibers, is somewhat different; and because of the fact that these nerves in this animal are largely employed for determining experimentally their respective actions on the heart, this relation should be clearly understood.

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[1] In man the annulus of Vieussens connects the inferior cervical with the middle cervical ganglion.

The *sympathetic* nerve-fibers in this animal are also in connection with the heart on the one hand and with nerve-fibers coming from the central nerve system on the other hand. The pre-ganglionic fibers take their origin very probably in nerve-cells in the medulla oblongata. From this origin they descend and emerge from the spinal cord in the anterior roots of the third spinal nerve, then pass through the white rami communicantes to the third sympathetic ganglion around the nerve-cells of which their terminal fibers arborize.

From the nerve-cells of this ganglion, the sympathetic nerves proper, the post-ganglionic, non-medullated fibers arise. From this origin they ascend, passing successively through the second sympathetic ganglion, the annulus of Vieussens, the first sympathetic ganglion, to the ganglion on the trunk of the vagus, at which point they enter the sheath of the vagus fibers and in company with them pass to the heart. For this reason the common trunk is generally spoken of as the *vago-sympathetic* nerve.

The *vagus* nerve is connected with the medulla oblongata by a series of from six to eight roots. A short distance from the medulla, the nerve trunk passes through a large opening in the cranium beyond which it presents an enlargement, termed the vagus ganglion. The peripheral end of this ganglion gives off two trunks, one the glossopharyngeal, the other the vagus proper.

The vagus nerve proper in the frog also consists of both afferent and efferent fibers which have practically the same origin, distribution and termination as the corresponding fibers in the mammal.

After the union of the sympathetic fibers with the vagus fibers, the common trunk passes forward to the angle of the jaw, winds around the pharynx just beneath the border of the petro-hyoid muscle and in close relation with the carotid artery. As the nerve approaches the heart it divides into two branches, the pulmonary and the cardiac. At the sinus venosus some of the fibers become related, histologically and physiologically, with the ganglion cells, while others plunge into the heart, course along the auricular septum on the left side and finally terminate at or near the ganglion cells of the base of the ventricle. The mode of termination of both the vagus and sympathetic fibers is similar to that observed in the mammals.

The Physiologic Actions of the Sympathetic Nerves in the Frog.—The information now possessed regarding the influence which the central nerve system exerts on the heart through these nerves, has been derived largely from experiments made on the nerves of the frog, toad, and turtle. Inasmuch as the sympathetic and vagus nerves in the frog and related animals are bound up in a common sheath, it is necessary in order to demonstrate their respective functions first to divide the nerves, above their union at the vagus ganglion, and then stimulate their peripheral ends. The heart should be exposed and attached to a recording lever so that its movements may be taken up and recorded on a moving recording surface.

Stimulation of the sympathetic fibers with induced electric currents, prior to their union with the vagus, is followed by an increase in the rate, or an augmentation in the force of the heart-beat or both, at the same time.

The effects of such a stimulation with induced currents of moderate intensity are graphically shown in Fig. 141. The upper tracing shows that the heart was first accelerated, the beats increasing from 15 per minute before stimulation, to 30 per minute during stimulation. On the cessation of the stimulation, the heart slowly returned to its former rate. Coincidently with this acceleration of the rate there was an augmentation of the force of the ventricular contraction as shown by an increase in the height of the ventricular contraction which before stimulation was 9 mm., but during stimulation 12 mm.

In addition to the foregoing changes in the heart-beat there is an alteration in the sequence of the beat. The natural delay in the conduction of the excitation process from the auricles to the ventricle is increased, in consequence of which the auricle completely relaxes before the ventricular contraction begins. Moreover, the auricular contraction again occurs before the ventricle has completely relaxed. After the effect of the stimulation passes away, the acceleration diminishes, the augmentation declines and a reverse change in the sequence occurs. The lower tracing shows a similar series of effects. If the stimulus be applied to the pre-ganglionic sympathetic nerves, an acceleration or augmentation of the heart follows, similar in all respects to that which follows stimulation of the post-ganglionic or sympathetic fibers proper; and the inference may be drawn that if the stimulus could be applied directly to the nerve-cells in the medulla oblongata from which the fibers take their origin, the same acceleration or augmentation would follow; for this reason this collection of nerve-cells is known as the *cardio-accelerator* or *augmentor* center. Since stimulation of the nerve in any part of its course, which in all probability exaggerates its normal function, is followed by an acceleration or an augmentation, the sympathetic is said

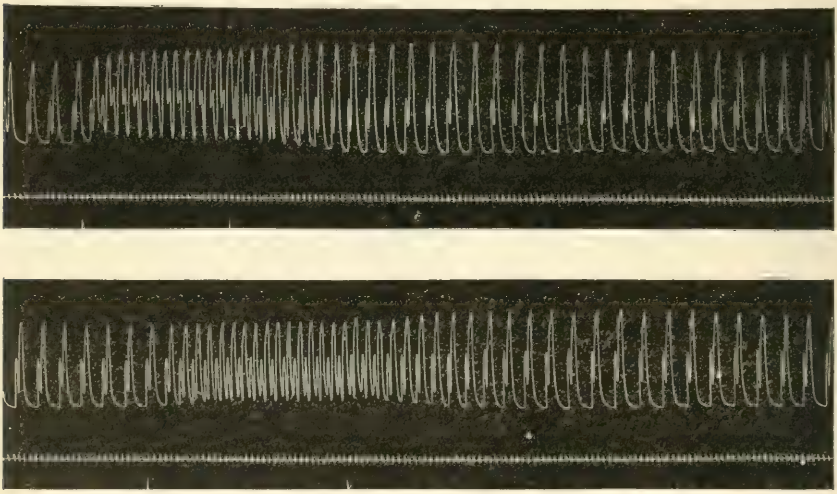

FIG. 141.—TRACINGS SHOWING THE EFFECTS ON THE HEART-BEAT OF THE FROG FROM STIMULATION OF THE SYMPATHETIC NERVES PRIOR TO THEIR UNION WITH THE VAGUS NERVE. The upper tracing shows an increase in the rate, which before stimulation was 15 per minute and during stimulation 30 per minute. Before stimulation the height of the ventricular beat was 9 mm. and during the stimulation it was 12 mm. The lowest tracing shows a similar series of effects, the differences being only of degree.—(*Brodie.*)

to have an accelerator or an augmentor influence on the heart-beat; with the cessation of the stimulation, and very frequently before, the heart returns to its normal condition.

The Physiologic Action of the Vagus Nerve in the Frog.—*Stimulation* of the intra-cranial roots of the vagus with very weak induced electric currents is followed by a gradual diminution in the rate and a diminution in the force of the heart-beat. If the induced currents are moderate in strength, the heart will at once come to a standstill in diastole. (Fig. 142.) If the stimulus be applied to the trunk or the peripheral portion of the vagus, for example close to the sinu-auricular junction, an inhibition occurs similar in all respects to that which follows stimulation of the intra-cranial roots, and judging from what is known regarding the action of nerve-cells, the inference may be drawn that if the stimulus could be applied directly to the group of nerve-cells from which the efferent fibers arise, the same inhibition would follow; for this reason this collection of nerve-cells is known as the *cardio-inhibitor* center. Since stimulation of the nerve, either at its center, in its course, or at its periphery, which in all probability exaggerates its normal function, is followed by a period of rest or inactivity, the vagus is said to have a retarding or an inhibitor influence on the beat of the heart.

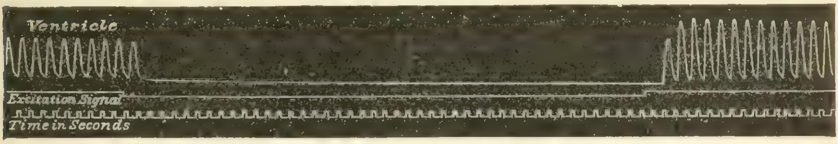

Fig. 142.—Tracing showing the Effect on the Heart-beat of the Toad of Long Stimulation of the Intra-cranial Roots of the Vagus with Moderately Strong Electric Currents.—(*Gaskell.*)

During the continuance of the inhibition, the heart-muscle is relaxed, its cavities dilated and filled with blood. The dilatation usually exceeds that observed prior to the vagus stimulation, from which it is inferred that some fibers of the vagus at least diminish the tonicity of the heart-muscle.

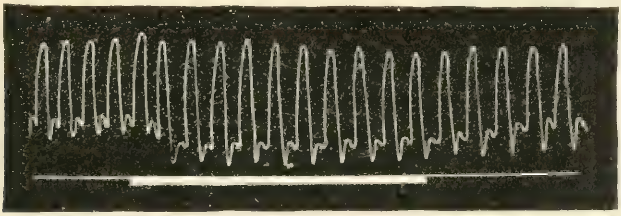

Fig. 143.—Tracing showing the Diminution in the Rate of the Heart-beat following Weak Tetanization of the Vagus Trunk.

After cessation of the stimulation, the heart resumes its activity. At first the beat usually is slow and feeble, but with each succeeding beat both the rate and force increase, until they attain or exceed that observed prior to the stimulation. In some cases, however, the heart begins to beat with as much and even more vigor than it did prior to the stimulation. The duration of the inhibitor effect varies with the duration of the stimulation. Thus during and after a stimulation of thirty-eight seconds the heart of the toad remained at rest for 292 seconds (Gaskell); the heart of a snake for from one-half to one hour (Meyer); the heart of a turtle for four and a half hours (Mills). The period of inhibition will depend on the strength of the electric current employed, the nerve stimulated, the season of the year, etc.

The effects on the heart-beat which will follow stimulation of the vago-sympathetic in its course vary, however, because of the antagonistic action of the inhibitor and accelerator nerve impulses. Thus stimulation of the peripheral end of the divided *trunk* of the vagus in the frog or the toad with weak tetanizing induced electric currents is followed by an increase in the rate of the heart-beat because of the stimulation of the accelerator fibers, which apparently respond before the inhibitor fibers; stimulation with somewhat stronger currents is followed by a diminution in the rate of the beat because of the greater effect on the inhibitor nerve-fibers (Fig. 143). Stimulation with strong tetanizing currents is followed by complete inhibition (Fig. 144).

The foregoing facts lead to the inference that the cardio-accelerator and the cardio-inhibitor centers have as their function the discharge of nerve impulses which are conducted by their related nerves, the efferent sympathetic and vagal fibers, to the heart, and which, in a manner, as yet unexplained accelerate or augment or inhibit, the action of the heart. The relation which these two centers bear one to the other and the manner in which they are influenced in their activities both directly and reflexly and thus regulate the action of the heart from moment to moment will be considered in a subsequent paragraph.

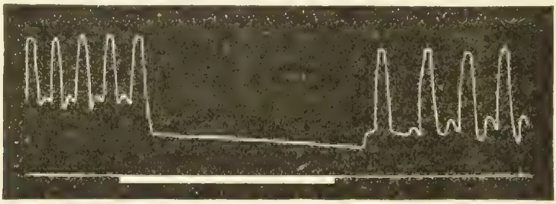

FIG. 144.—TRACING SHOWING COMPLETE INHIBITION FOLLOWING STRONG TETANIZATION OF THE VAGUS TRUNK.

Changes in the Conductivity of the Heart.—In addition to the changes in the rate and force of the heart caused by stimulation of the inhibitor and the augmentor nerves, it is stated by Gaskell that there is also during the inhibition a *decrease* in the conductivity of the heart at both the sino-auricular and auriculo-ventricular junctions, and an *increase* in the conductivity during acceleration of the beat. The decrease in conductivity may be so pronounced that only every second or third contraction of the auricle will be followed by a contraction of the ventricle. In other instances both auricles and ventricles remain at rest while the sinus maintains its usual rate. The increase in conductivity is shown by first artificially blocking the contraction wave at the auriculo-ventricular junction with the clamp, until only every second or third auricular contraction is conducted to the ventricle, and then stimulating the sympathetic. At once the auricular contraction forces the block, and passes to the ventricle, calling forth a normal contraction.

The Physiologic Actions of the Sympathetic Nerves in Mammals.—In the mammal the actions of the sympathetic nerves closely resemble their action in the frog. Thus *stimulation* of the nerves in any part of their course, either through the rami communicantes, or after their emergence from either the stellate or the inferior cervical ganglion is followed by effects similar to those observed in the frog: viz., an acceleration or augmentation, or both, of the heart-beat. The percentage increase in the acceleration varies in different animals. In some instances the increase varies from 58 per cent. to 100 per cent. (Hunt). If the heart is beating slowly before stimulation, the acceleration is more marked than if it is beating rapidly.

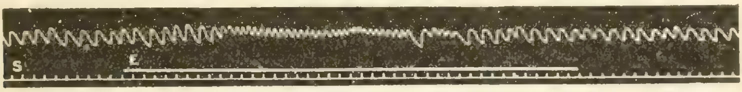

FIG. 145.—ACCELERATION OF THE HEART-BEAT FOLLOWING STIMULATION OF THE CARDIAC BRANCHES WHICH COME FROM THE ANNULUS OF VIEUSSENS.

The effect of the accelerator impulses is apparently a change in the inner mechanism of the heart-muscle itself and not a change in the peripheral portion of the inhibitor apparatus. This is indicated by the fact that acceleration occurs after the full physiologic action of atropin, which acts upon, and impairs the conductivity of the intra-cardiac nerve-cell (post-ganglionic) terminals.

A peculiarity of the sympathetic nerve is that it does not respond to stimulation as rapidly as do many nerves, so that a rather long latent period intervenes between the moment of stimulation and the appearance of the acceleration as shown in Fig. 145. A further peculiarity is that the acceleration sometimes continues after the stimulus is withdrawn, and sometimes ceases before it is withdrawn.

The force of the heart-beat may be increased without there being any increase in the rate (Fig. 146). The auricular contraction is probably increased whereby the ventricle is more completely filled.

Though an increase in both the rate and force frequently occur simultaneously, there is no necessary relation or connection between the two as they can and do occur independently of each other. For this reason it is generally assumed that the sympathetic nerves contain two groups of fibers, viz., accelerators and augmentors, the functions of which are respectively to accelerate the rate and augment the force of the heart-beat. From the fact that both auricles and ventricles exhibit these changes it is assumed that the nerve impulses stimulate both chambers. This is rendered probable also from the experiments of Erlanger, who found that after complete heart-block, stimulation of the sympathetic caused independent acceleration of both auricles and ventricles.

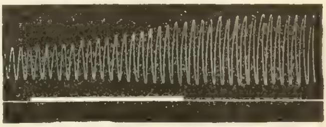

FIG. 146.—INCREASE IN THE FORCE OF THE VENTRICULAR CONTRACTION (CURVE OF PRESSURE IN RIGHT VENTRICLE) FROM STIMULATION OF AUGMENTOR FIBERS. There is little or no change in frequency.—(*Franck, reduced.*)

Division of the sympathetic nerves is at once followed by a diminution in the rate, the degree of which will depend to some extent on the rate at which the heart was beating prior to the division. The results therefore that follow stimulation and division of these nerves indicate that they are transmitting nerve impulses from the centers from which they arise to the heart upon which they exert a stimulating influence on the rate and force of the beat.

The Physiologic Action of the Vagus Nerve in Mammals.—In the mammal the same or similar effects in varying degree result from stimulation of the vagus as in the frog. These results can be readily shown in the dog or rabbit in the following way. The thorax of the animal is opened and artificial respiration maintained. Under these circumstances the heart will continue to beat in a practically normal manner for a long time. The vagus nerve is then exposed on one side and divided, and its peripheral end stimulated with induced electric currents of moderate strength; whereupon the heart will come to a standstill almost immediately in the condition of diastole, and may be so kept for a variable period, from fifteen to thirty seconds or more, during which its walls are relaxed and its cavities filled with blood. On cessation of the stimulation the contractions return and in a very short time the former rate and force of the beat are regained. If the electric currents are of feeble strength, the heart will come to rest gradually, through a gradual diminution in the rate and force of the contraction. During the period of the inhibition the heart presents an appearance similar to that presented by the heart of the cold-blooded animal, viz.: completely relaxed walls and the cavities filled and distended with blood. When the heart of an animal is thus exposed, the auricle and the ventricle of one side may be attached by threads to writing levers and their contractions registered on a moving recording surface. The effects on both auricles and ventricles which follow vagus stimulation will then become more apparent. Fig. 147 is a tracing thus obtained. The animal employed for the experiment was a rabbit.

Division of one vagus is followed in some mammals, *e.g.*, dog by a marked increase in the rate of beat and if both vagi are divided the increase may amount to from 50 to 75 per cent. The results of stimulation and division of the vagus nerves indicate that they are continuously transmitting nerve impulses from the centers from which they arise, to the heart-muscle, on the activity of which they exert a restraining or inhibitor influence.

The inhibitor effect of the vagus varies in degree and duration in different animals. In the dog the effect of vagus stimulation is usually pronounced, lasting from 15 to 30 seconds; in the rabbit it is perhaps equally well pronounced but somewhat less in duration; in the cat it is frequently wanting. In this latter animal a complete standstill, even for a few seconds, is very rarely seen; usually there is produced merely a slight diminution in the rate of the beat even though the stimulus employed is quite strong. In all these animals, however, after a very short time the nerve impulses lose their inhibitor influence on the heart-muscle, and notwithstanding continued stimulation of the vagus, the heart returns to its former rate and vigor. This result is in marked contrast to that observed during stimulation of the vagus in the cold-blooded animals, in which the heart may be kept at rest for relatively very long periods of time. No satisfactory explanation for this loss of vagus control or escape of the heart from the vagus control has as yet been offered.

Seat of Action of the Vagus Impulses.—In the foregoing experiment of which Fig. 147 is a graphic record, stimulation of the left vagus with a fairly strong current was followed by a diminution in both the rate and force of the contraction of both auricles and ventricles, though the effect was most marked in the auricles. From this and similar facts it has come to be the general belief that the inhibitor nerve impulses exert their influence mainly, if not exclusively, on the auricle, and especially on the sino-auricular node, and that the cessation of ventricular action is a secondary effect due to the non-arrival across the conducting apparatus of the normal excitation process from the auricle. This is the case undoubtedly in the cold-blooded animals, and the experiments of Erlanger on the heart of the dog indicate that the same holds true for the mammals. This investigator has found that when the auriculo-ventricular tissues are suddenly clamped, including presumably the muscle bundle of His, there is for a time a complete cessation of ven-

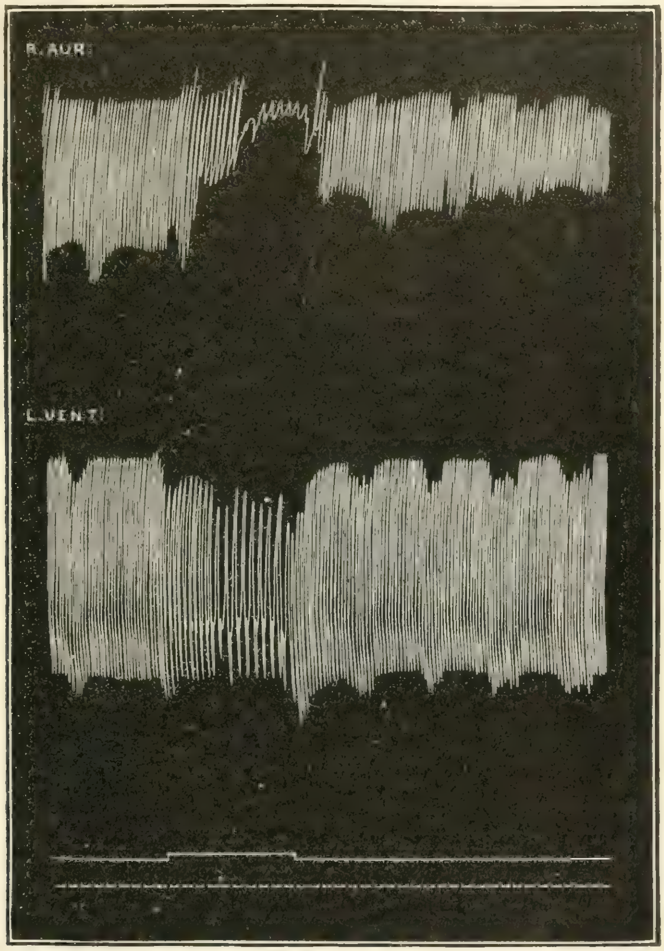

FIG. 147.—RESULT OF THE STIMULATION OF THE PERIPHERAL END OF THE DIVIDED LEFT VAGUS IN THE RABBIT.—(*Brodie.*)

tricular activity, but after a variable period of time, fifty seconds or more, the ventricle develops an independent rhythm which gradually increases in frequency, but seldom, if ever, attains that of the auricles. Under such circumstances tetanic stimulation of the auriculo-ventricular tissues by means of the clamp now transformed into stimulating electrodes, failed to bring about a stoppage of the ventricles. Moreover, if during the time the clamp is applied and after the ventricle has developed a rhythm of its own, the vagus is stimulated, the auricles will cease to beat as usual, but the ventricles will continue to beat at their usual rate. These and similar facts lead to the conclusion that vagal inhibitor action is limited to the auricles.

From foregoing facts it is apparent that the accelerator and augmentor effects of the sympathetic nerve impulses, and the inhibitor effects of the vagus nerve impulses, closely resemble on the one hand, the accelerator and augmentor effects of increasing amounts of diffusible calcium salts, and on the other hand, the inhibitor effects of increasing amounts of diffusible potassium salts in the blood or other circulating fluid; and so closely do these two sets of phenomena resemble each other, that they are by some observers regarded as identical.

Some additional facts in this connection have been presented by Howell, viz., that an increase (within limits) and a decrease in the percentage of diffusible calcium salts in a circulating fluid passing through the cavities of the mammalian (cat) heart, increases on the one hand, and decreases on the other hand, the sensitiveness of the heart to sympathetic acceleration and augmentation. From this the inference is deduced that the acceleration and augmentation of the heart-beat which follow stimulation of the sympathetic nerves are due to the presence in the heart tissue of a certain percentage of diffusible calcium salts, which have been freed from combination with organic matter by the action of the sympathetic nerve impulses. Again, that an increase (within limits) and a gradual decrease in the percentage of diffusible potassium salts in a circulating fluid passing through the cavities of the frog and the cat heart, increases on the one hand and decreases and finally abolishes on the other hand the sensitiveness of the heart to vagus inhibition. From this the inference is deduced that the inhibition of the heart-beat which follows stimulation of the vagus nerve is due to the presence in the heart tissue of a certain percentage of diffusible potassium salts, which have been freed from combination with organic matter by the action of the vagus nerve impulses.

The foregoing effects of the sympathetic and vagus nerves on the heart muscle, viz.: changes in its irritability, conductivity, rapidity, and the energy of the beat, have been termed by Engelmann *bathmotropic*, *dromotropic*, *chronotropic*, and *inotropic*. Any one of these effects, *e.g.*, the chronotropic, may be modified in a positive direction by the sympathetic, or in a negative direction by the vagus.

The Cardio-accelerator Center.—The collection of nerve-cells from which the pre-ganglionic fibers of the sympathetic system arise is known as the cardio-accelerator or augmentor center. The exact location of this center in the central nerve system has not been as yet accurately determined. It is probably located in the medulla oblongata.

From experiments which have been made on the sympathetic nerve apparatus in its entirety, it is believed that the *function* of this center is the discharge of nerve impulses which, conducted to the heart by the preganglionic and post-ganglionic sympathetic fibers, cause an acceleration in the rate or an augmentation in the force, or both, of the heart-beat. It is also generally believed since the publication of Hunt's investigations that this center is in a state of tonic activity. This is shown by the fact that after the division of the vagus nerves and the removal of all possible inhibitor influences, division of the sympathetic nerves or extirpation of the stellate or inferior cervical ganglion, is yet followed by a *decrease* in the rate of the heart-beat. After division of the sympathetic nerves and the removal of accelerator influences it is also easier to bring about inhibition through vagus stimulation.

The Factors which Determine the Activity of the Cardio-accelerator Center.—The question has been raised as to whether the tonic activity of this center is maintained by *central* or *peripheral* stimuli, *i.e.*, whether it is maintained by causes within itself, the result of an interaction between the constituents of the cell substance and those of the surrounding lymph, or whether it is maintained by nerve impulses reflected to it through various afferent or sensor nerves. Inasmuch as there is no way of determining whether the causes are central, except by dividing all afferent nerves, it is impossible to state how much influence is to be attributed to this factor. On the contrary, though it is readily demonstrable that stimulation of many afferent nerves will cause an acceleration of the heart it cannot be stated positively that this is the result of a reflex stimulation of the accelerator center. Though earlier investigators believed this to be the correct interpretation, the more recent experiments of Hunt apparently disprove it; for this investigator has shown that if the vagus nerves are divided it is impossible to produce reflex acceleration of the heart. His conclusion, confirming that of others, is that cardiac acceleration is the result of an *inhibition* of the cardio-inhibitor center. A freer play to the tonic activity of the accelerator center would thus be made possible.

The Cardio-inhibitor Center.—The collection of nerve-cells from which the small efferent fibers of the vagus nerve arise is known as the *cardio-inhibitor* center.[1] It is situated in the medulla oblongata or more exactly in the gray matter beneath the floor of the fourth ventricle near the tip of the calamus scriptorius. It is in all probability a part of the nucleus ambiguus.

From the experiments which have been made on the vagus inhibitor apparatus in its entirety it is believed that the *function* of this center is the discharge of nerve impulses which conducted to the heart by the vagus fibers cause an inhibition of its beat of greater or less extent. In the dog, and probably in many other mammals, this center exerts a more or less constant inhibitor or restraining influence on the heart's activity. This is indicated by the fact that the rate of the beat is very much increased by simultaneous division of both vagi. The degree of the inhibition which this center exerts varies greatly, however, in different animals. In the cat and in the rabbit the inhibitor control is normally so slight that there is but a relatively slight increase in the rate of the beat after division of the vagi. The tone of the vagus in these animals is, therefore, said to be slight or feeble. In human beings the tone of the inhibitor apparatus is poorly developed in early childhood, as shown by the fact that the administration of atropin, which removes temporarily inhibitor control, is not followed by an increase in the rate of the beat. It develops steadily and reaches a maximum at from the twenty-fifth to the thirtieth year. In advanced years the tone again declines. For these and other reasons it is believed that this center is in a state of tonic activity in many if not all mammals, discharging nerve impulses which exert a regulative influence on the cardiac mechanism in accordance with its needs and especially in reference to the variable resistances offered to the flow of blood which the heart must overcome.

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[1] Inasmuch as the nerve system is bilaterally arranged there are of course two nerve-centers here as elsewhere, one on each side of the median line though they are associated in action by either commissural fibers or by a decussation of some of their efferent fibers.

The Factors which Determine the Activity of the Cardio-inhibitor Center.—The question has also been raised as to whether the tonic activity of this center is maintained by *central* or *peripheral* stimuli, *i.e.*, whether it is maintained by causes within itself the result of an interaction between the constituents of the cell substance and those of the surrounding lymph, or whether it is maintained by nerve impulses transmitted to it through various afferent or sensor nerves. Though both factors play an important part in the maintenance of its activity, it is difficult to state which is the more important of the two. That nerve impulses transmitted to the center through afferent nerves lead now to an inhibition, now to an acceleration of the heart has been abundantly established by the stimulation of afferent nerves in almost any region of the body. Thus stimulation of the dorsal roots of the spinal nerves, the trunks of the cranial sensor nerves, the splanchnic nerves, the pulmonary branches of the vagus, etc., gives rise to a more or less pronounced inhibition of the heart. On the other hand stimulation of afferent nerves sometimes leads to the opposite result, namely, acceleration of the heart. As a rule, stimulation of the peripheral terminations of these nerves is more effective than stimulation of their trunks. From facts such as these, it has come to be believed that nerve impulses developed in many regions of the body are being constantly transmitted to this center, which not only stimulate it to activity but modify its activity in one direction or another from moment to moment.

The first explanation, that acceleration of the heart, the result of a peripherally acting stimulus, is due to a stimulation of the cardio-accelerator center by the arrival of nerve impulses coming through afferent nerves, having been made questionable and improbable by the results of Hunt's experiments, the alternative explanation must be that while inhibition of the heart is due to an *excitation* of the normal activity of the cardio-inhibitor center, the acceleration of the heart is due to an *inhibition* of the normal activity of the cardio-inhibitor center, and hence there follows the corollary that afferent nerves contain two sets of nerve-fibers which are in physiologic relation with the cardio-inhibitor center, one of which when stimulated peripherally excites or augments its activity, the other of which when stimulated inhibits or depresses its activity, thus giving rise to a freer play of the cardio-accelerator center.

The extent to which both sets of fibers are present in any one afferent nerve is unknown. In the trigeminus it is believed the excitator fibers preponderate for the reason that peripheral stimulation of this nerve is followed by inhibition of the heart; in the sciatic, it is believed the inhibitor nerves preponderate, for the reason that stimulation of the central end of the divided nerve is followed generally by acceleration of the heart.

It is probable from the effects which follow gastro-intestinal disorders, that the vagus nerve contains both classes of fibers as represented in Fig. 141, inasmuch as stimuli of a pathologic character in one individual may reflexly excite or increase the activity of the cardio-inhibitor center, to be followed by an inhibition of the heart; and in another individual, may reflexly inhibit the activity of the same center and to such an extent that the cardio-accelerator center may be enabled to increase either the rate or the force or both, of the heart movements. Palpitation of the heart from gastric irritation might thus be explained.

From the results of stimulation of the sympathetic (accelerator) and vagus (inhibitor) nerves under a great variety of conditions it has been established that their respective centers are mutually antagonistic; that the activity of the accelerator center at one moment limits the activity of the inhibitor and at another moment is limited in turn by it; that the rate of the heart-beat at each moment is the resultant of the relative degree of activity of the two centers.

The Influence of Psychic States.—It is a familiar personal experience that emotional states, according to their suddenness or intensity may increase or decrease the activity of the heart; thus depressing emotions may diminish the activity almost to the point of complete inhibition, while joyous emotions on the contrary may increase both rate and force to the point at which the action becomes tumultuous and even irregular. The effects in either case are due to nerve impulses descending from the cerebrum to the cardiac center in the medulla.

The nerve impulses discharged by cerebral cells during the occurrence of both the depressing and joyous emotions exert their influence in all probability, on the cardio-inhibitor center alone. In the case of depressing emotions, the nerve impulses *excite* or increase the normal degree of activity of this center in consequence of which its inhibitor influence on the heart is increased; in the case of joyous emotions, the nerve impulses *inhibit* the normal degree of activity of the center in consequence of which its influence on the heart is decreased. This permits of a freer play of the cardio-accelerator center and as a result there is an increased activity of the heart.

The Causes of the Variations in the Heart-beat.—It has been stated elsewhere in the text (page 290), that the rate of the heart-beat is influenced by age, muscle activity, the position of the body, meals, variations in blood pressure, etc. The manner in which these changes are brought about is not, however, always apparent. In addition to variations that are strictly physiological in character there is abundant evidence that other factors, *e.g.*, the action of peripheral stimuli of a physiologic or pathologic character in various regions of the body, can and do cause reflexly at one time or in one individual an acceleration of a marked character, and at another time or in another or the same individual an inhibition which may be so pronounced as to almost lead to a complete, though temporary standstill of the heart in diastole. The records of clinical medicine contain many instances which show that ocular, dental, gastric, intestinal, uterine and other organic disorders, as well as various operative procedures in different regions of the body cause now an acceleration, now an inhibition of the heart which may be so marked and pronounced as to give rise to serious apprehensions.

The Depressor Nerve.—The vagus trunk also contains afferent fibers stimulation of which not only brings about a reflex inhibition of the heart, but also a dilatation of the peripheral arteries and a fall of blood-pressure through a depressive influence on the vaso-motor centers. To this nerve the term depressor has been given. A consideration of the physiologic action of this nerve will be found in the section devoted to the nerve mechanisms concerned in the maintenance of the blood-pressure.

Modifications of the Nerve Mechanism of the Heart that Follow Slightly Toxic Doses of Drugs.—The functions of different parts of the nerve mechanism of the heart may be demonstrated by an analysis of the effects that follow the administration of slightly toxic doses of the alkaloids of various drugs. The effects can be shown to be due to a stimulation or to a depression of the normal activity of one or more portions of the mechanism. The alkaloid may exert its specific action on the central portions in the medulla, or on the peripheral portions in the heart, or on both simultaneously. The heart-muscle may at the same time be stimulated or depressed in its action either in the same or in the opposite direction to that of the nerve mechanism. As a result the heart-beat may be increased or decreased both in rate and force.

The following examples will illustrate the action of alkaloids in general.

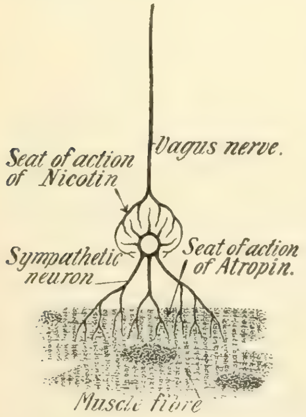

Fig. 148.—Diagram showing the Relation of the Vagus to the Heart-muscle Cell.

Atropin.—After the administration of atropin in sufficient amounts the heart-beat increases in frequency in all animals in which the cardio-inhibitor centers exert a steady inhibitor influence over the heart. This is especially true in man and the dog. In animals in which the inhibitor control is slight, as the rabbit and frog, the increase in frequency is not very marked. In all animals thus far experimented on after the administration of atropin, neither stimulation of the trunk of the vagus nor stimulation of the intracardiac ganglia will arrest or even retard the heart-beat. The inference, therefore, is that the alkaloid exerts its action upon the ganglion cells and their terminal branches, impairing their chemic integrity and abolishing their normal function, that of conducting nerve impulses from the vagus nerve proper to the heart-muscle. Fig. 148. In consequence of this, the influence of the cardio-inhibitor center is cut off and the cardio-accelerator being unopposed in its activity, the rate of the beat is increased. After a variable period the heart returns to its normal rate. Stimulation of the vagus is again followed by the usual inhibition. As atropin is partly oxidized, and partly excreted, it is assumed that the nerve terminals have been restored by nutritive forces to their normal condition and their conductivity regained. This having been accomplished the vagus nerve impulses can again reach the heart-muscle and the cardio-inhibitor center is, therefore, enabled to re-establish inhibitor control and antagonize the activity of the cardio-accelerator center.

Nicotin.—After the administration of nicotin in sufficient amounts the heart-beat is primarily decreased in frequency even to the point of standstill in diastole for a few seconds, and secondarily increased both in frequency and force beyond the normal. If the vagus nerves be first divided this primary decrease is not so marked and the inference is that the alkaloid primarily stimulates the cardio-inhibitor center and increases its normal function and perhaps the terminal branches of the vagus fibers, the pre-ganglionic, as well. After the secondary increase in the rate is established stimulation of the vagus trunk fails to inhibit the heart, though stimulation of the intra-cardiac ganglia is at once followed by the usual inhibitor phenomenon, arrest of the heart in diastole. For this reason it is believed that nicotin acts on the peripheral terminations of the pre-ganglionic fibers of the vagus as they arborize around the intra-cardiac ganglia, depressing them and suspending their normal function, that of conducting nerve impulses from the vagus to the ganglion cells. Since stimulation of the pre-ganglionic fibers of the accelerator apparatus fails to accelerate the rate of the heart-beat, though stimulation of the post-ganglionic fibers has the usual accelerating effect, the inference is that nicotin acts upon and suspends the conductivity of their terminal branches in the ganglia. The acceleration of the heart must therefore be attributed either to a stimulation of the post-ganglionic fibers or of the cardiac muscle itself (Cushny).

Pilocarpin and Muscarin.—These alkaloids, whether administered internally or applied locally to the heart, diminish the frequency and the force of the beat to such an extent that it very shortly comes to rest in diastole. For the reason that the internal administration or the local application of atropin in proper doses, which has a depressive action on the intra-cardiac cell terminations, removes the inhibition and restores the normal rhythm, the inference is drawn that both these alkaloids either increase the irritability of the nerve-cells or heighten the conductivity of their terminal fibers. The return of the heart-beat is attributed to a decline in irritability to the normal level in consequence of the antagonistic action of the atropin.

Digitalin.—The administration of digitalin gives rise to effects the character and extent of which vary in different animals. In the frog, as a rule, the only effect produced is a gradual increase in the duration and force of the ventricular systole, with a corresponding decrease in the duration of the diastole, until the heart comes to rest in the systolic state. As this effect is observed after division of the vagus trunk and also after the suspension of the activity of the intra-cardiac cell-fibers by atropin, it is evidently due to a direct stimulation of the heart-muscle. In some instances, however, the opposite effect is produced, viz.: a gradual increase in the length of the diastole a decrease in the duration of the systole, until the heart comes to rest in the diastolic state. As this effect arises only when the vagus nerve is intact it is very probably due to a stimulation of th e cardio-inhibitor center and a consequent increase of its functional activity. Though either effect may be produced in the frog the predominant effect is the increase in the contraction of the heart-muscle rather than an inhibition of the beat.

In mammals both effects are observed, viz.: a diminution in the rate of the beat, a lengthening of the diastole and an increase in the vigor of the systole, which are evidently due to a simultaneous stimulation of the cardio-inhibitor center and of the cardiac muscle. Digitalin thus expends itself on two opposing mechanisms; as to which gains the ascendency will depend on the dosage and the character of the animal.

CHAPTER XIV

THE CIRCULATION OF THE BLOOD (Continued)

THE VASCULAR APPARATUS: ITS STRUCTURE AND FUNCTIONS

The Vascular Apparatus in its entirety consists of a closed system of vessels which not only contain the blood, but under the driving power of the heart, transmit it to and from all regions of the body. It is usually divided into a systemic and a pulmonic portion.

The Systemic Vascular Apparatus.—This portion of the general vascular apparatus includes all the vessels extending from the left ventricle to the right auricle: viz., the arteries, capillaries, and veins. Though serving as a whole to transmit blood from the one side of the heart to the other, each one of these three divisions has separate but related functions, which are dependent partly on differences in structure and physiologic properties, and partly on their relation to the heart and its physiologic activities.

The Structure, Properties and Functions of the Arteries.—The arteries serve to transmit the blood ejected from the heart to the capillaries; that this may be accomplished they divide and subdivide and ultimately penetrate each and every area of the body. Their repeated division is attended by a diminution in size, a decrease in the thickness and a change in the structure of their walls.

A typical artery consists of three coats: an internal, the *tunica intima;* a middle, the *tunica media;* an external, the *tunica adventitia.*

The internal coat consists of a structureless elastic basement membrane, the inner surface of which is covered by a layer of elongated spindle-shaped endothelial cells. The middle coat consists of several layers of circularly arranged, non-striated muscle-fibers, between which are networks of elastic fibers. The external coat consists of bundles of connective tissue of the white fibrous and yellow elastic varieties. Between the external and middle coats there is an additional elastic membrane. In the small arteries there is but a single layer of muscle-fibers. In the large arteries the elastic tissue is very abundant, exceeding largely in amount the muscle-tissue. It is also more closely and compactly arranged. The external coat is well developed in the large arteries (Fig. 149).

The presence in their walls of both elastic and contractile elements, endows the arteries with the two properties of elasticity and contractility.

Elasticity.—The elasticity is best developed in the large arteries, though it is also present in arteries of relatively small size. By virtue of the elasticity, the arteries are capable of being distended and elongated and when the distending force is removed of recoiling or retracting and returning to their former condition. Thus the capacity of the aorta and carotid artery of the rabbit can be increased four times and six times respectively by raising the intra-arterial pressure from 0 to 200 mm. of mercury. The elasticity permits of a wide variation in the amount of blood the arterial system can hold between its minimum and maximum distension. The arteries thus adapt themselves to the variations in the volume of blood discharged from the ventricle at a single beat or in a unit of time. The elasticity also converts the intermittent movement of the blood imparted to it by the heart as it is ejected from the ventricle, into a remittent movement in the arteries and finally into the continuous and equable movement observed in the capillaries. This is accomplished in the following manner: With each contraction of the left ventricle more blood is ejected into the aorta than the arteries can discharge into the capillaries and veins during the time of the contraction, owing to the small caliber and friction of the arterioles. The portion not so discharged exerts a lateral pressure against the walls of the arteries which at once dilate until a condition of equilibrium is established between the pressure from within and the elastic reaction of the arterial walls from without. With the cessation of the contraction the elastic walls recoil and propel the blood toward the capillaries. The intermittent action of the heart is thus succeeded by the continuous reaction of the arterial wall.

As the blood advances toward the periphery of the arterial system and larger amounts pass into the capillaries, both the distention and the elastic recoil diminish, and by the time the blood reaches the capillaries its intermittency of movement has been so far obliterated by the elastic recoil that as it enters the capillaries the movement becomes equable and continuous. In this manner the arteries modify and change the character of the blood flow and in part adapt it for the conditions of the blood flow in the capillary vessels.

In youth the arterial walls are highly distensible and elastic; in advanced years they are frequently relatively rigid and inelastic, and in consequence the flow of blood toward and into the capillaries approximates in its characteristics the flow of a fluid through a rigid tube under the intermittent action of a pump; that is, the intermittent movement imparted by the heart is not so completely converted into a continuous movement, and hence the blood flows through the capillaries during the systole with greater velocity, and during the diastole with less velocity, than is the case when the vessel is normally elastic. For these and other reasons the tissues are not so well nourished and hence their nutrition and functional activities decline.

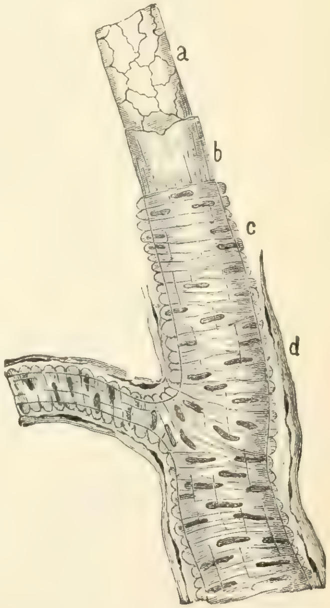

FIG. 149.—COATS OF A SMALL ARTERY. *a.* Endothelium. *b.* Internal elastic lamina. *c.* Circular muscular fibers of the middle coat. *d.* The outer coat.—(*Landois and Stirling.*)

Contractility.—The contractility permits of a variation in the amount of blood passing into a given capillary area in a unit of time. Normally each artery has a certain average caliber due to a given contraction of the muscle coat. Beyond this average condition the artery can pass in one direction or the other by either a relaxation or increased contraction of the muscle coat. During the functional activity of any organ or tissue there is need for an increase in the amount of blood beyond that supplied during functional inactivity or rest. This is accomplished by a relaxation of the muscle-fibers. With the cessation of activity the muscle-fibers again contract and reduce the amount of blood to that required for nutritive purposes only. An increased contraction of the muscle-fibers beyond the average, diminishes the outflow of blood, and if sufficiently great may give rise to anemia and pallor. The contractile elements at the periphery of the arterial system, in the so-called *arteriole* region, therefore regulate the supply of blood to the tissues in accordance with their functional needs.

Moreover, as will be stated in subsequent paragraphs the degree of contraction of the arteriole muscle influences very markedly the degree of friction which the blood has to overcome in passing from the arteries into the capillaries. If the muscle contracts vigorously the caliber of the arteriole is diminished and the friction increases; if the muscle relaxes, the caliber of the arteriole is enlarged and the friction decreases. By virtue of its tonic activity, the arteriole muscle at the periphery of the arterial system offers considerable resistance to the outflow of the blood and this is therefore spoken of generally, as the *peripheral resistance,* though there is included under this term the resistance offered by the small caliber of the capillary blood-vessel as well. This latter factor is constant, the former variable.

The *functions* of the arteries therefore are as follows: (1) to distribute the blood to all regions of the body; (2) to accommodate varying volumes of blood; (3) to convert the intermittent flow of blood as it leaves the heart into a remittent and finally into a continuous and equable flow as it passes into the capillaries; (4) to regulate the volume of blood delivered to an organ in accordance with its functional activities, and (5) to present that degree of resistance necessary to the maintenance of the normal blood pressure, through the activities of the muscle fibers in the walls of the arterioles.

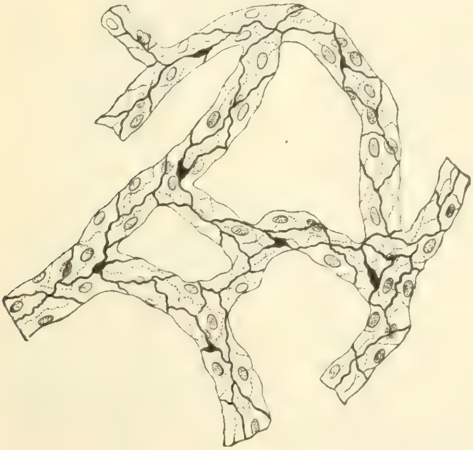

FIG. 150.—CAPILLARIES. THE OUTLINES OF THE NUCLEATED ENDOTHELIAL CELLS WITH THE CEMENT BLACKENED BY THE ACTION OF SILVER NITRATE.—(*Landois and Stirling.*)

The Structure, Properties, and Functions of the Capillaries.—The capillaries are small vessels continuous with the arteries on the one hand and with the veins on the other hand. Though different in structure from a small artery or vein, there is no sharp boundary between them, as their structures pass imperceptibly one into the other. A true capillary, however, is of uniform size in any given tissue and does not undergo any noticeable decrease in size from repeated branchings. The diameter varies in different tissues from 0.0045 mm. to 0.0075 mm., just sufficiently large to permit the easy passage of a single red corpuscle. The length varies from 0.5 mm. to 1 mm. The wall of the capillary (Fig. 150) is composed of a single layer of nucleated endothelial cells with serrated edges united by a cementing material. Though extremely short, the capillaries divide and subdivide a number of times, forming meshes or networks, the closeness and general arrangement of which vary in different localities.

As the endothelial cells are living structures and characterized by irritability, contractility and tonicity, it may be assumed that the capillary wall as a whole is characterized by the same properties. Upon the possession of these properties the functions of the capillary depend.

The *function* of the capillary wall is to permit of a passage of the nutritive materials of the blood into the surrounding tissue spaces and of waste products from the tissue spaces into the blood. The structure of the capillary wall is well adapted for this purpose. Composed as it is of but a single layer of endothelial cells, the thickness of which defies accurate measurement, it readily permits, under certain conditions, of the necessary exchange of materials between the blood and the tissues. The forces which are concerned in the passage of materials across the capillary wall are embraced under the terms *diffusion*, *osmosis*, and *filtration*. As a result of the interchange of materials the tissues are provided with nutritive materials and relieved of the presence of the products of metabolism. As the blood loses oxygen and gains carbon dioxid, it changes in color from a scarlet red to a bluish red. In consequence of the exchange of materials, the blood undergoes a change in composition, the extent and character of which varies in accordance with the activities and character of the organ traversed by it.

In order that the nutritive materials may pass through the capillary wall in amounts sufficient to maintain the necessary supply of lymph in the lymph or tissue spaces, it is essential that the blood shall flow into and out of the capillary vessels constantly and equably, in volumes varying with the activities of the tissues, under a given pressure and with a definite velocity. These conditions are made possible by the coöperation of the physiologic properties and physiologic actions of the heart and vascular apparatus, the nature of which will be explained in subsequent pages.

The Structure, Properties, and Functions of the Veins.—The veins arise from the distal side of the capillary vessels. As they emerge they are quite small and designated venules. By their convergence and union the the veins gradually increase in size in passing from the periphery toward the heart. Their walls at the same time correspondingly increase in thickness. The veins from the lower extremities, the trunk, and abdominal organs finally terminate in the inferior vena cava. The veins from the head and upper extremities terminate in the superior vena cava. Both venæ cavæ empty into the right auricle.

A typical vein consists of the same three coats as the artery: viz., the *tunica intima*, the *tunica media*, and the *tunica adventitia*. The *media*, however, does not possess as much of either the elastic or muscle tissue as the artery, but a larger amount of the fibrous tissue. Hence they readily collapse when empty. In virtue of their structure the veins also possess both *elasticity* and *contractility*, though in a far less degree than the arteries. These properties come into play and are of value in furthering the movement of the blood toward the heart, especially after a temporary obstruction.

Certain veins, especially the large veins of the extremities, are characterized by the presence of valves throughout their course. These are arranged in pairs and formed by a reduplication of the internal coat, strengthened by fibrous tissue. They are always directed toward the heart and in close relation to the walls of the veins, so long as the blood is flowing forward. An obstruction to the flow causes the valves to turn backward until they meet in the middle line, when they act as a barrier to regurgitation. Under these circumstances the elastic tissue permits the veins to distend and accommodate the blood. With the removal of the obstruction the recoil of the elastic tissue, and perhaps the contraction of the muscle-tissue, forces the blood quickly onward. The veins of many viscera, of the bones, of the cranial and vertebral cavities are devoid of valves. The *function* of the veins is therefore to collect the blood from the capillary areas and transmit it to the heart.

THE FLOW OF THE BLOOD THROUGH THE VESSELS
HYDRODYNAMIC CONSIDERATIONS

The blood flows through the arteries, capillaries and veins in accordance with definite laws. During its transit certain phenomena are presented by each of these three divisions of the vascular apparatus. These are mainly velocity and pressure and in the arteries alone an alternate expansion and recoil of the arterial wall with each heart beat, termed the pulse. Since these phenomena, as well as the laws which govern them are similar to, though more complex than the phenomena presented by relatively simple tubes with rigid or elastic walls while liquids are flowing through them under a steadily acting or an intermittently acting pressure, it will be conducive to clearness of conception of the mechanics of the vascular apparatus, if there be considered:

1. The flow of a liquid through a horizontal tube with rigid walls and of uniform or variable diameter under a steadily acting pressure.
2. The flow of a liquid through a series of branching and again uniting tubes with rigid walls under a steadily acting pressure.
3. The flow of a liquid through a tube with elastic walls under an intermittently acting pressure.

THE FLOW OF A LIQUID THROUGH A HORIZONTAL TUBE WITH RIGID WALLS UNDER A STEADILY ACTING PRESSURE

The phenomena and the laws which govern them, that attend the flow of a liquid through a rigid tube of uniform diameter under a steadily acting pressure may be readily observed in an apparatus similar to that represented in Fig. 151, which consists of a horizontal tube into which is inserted at equal distances a series of vertical tubes, and which is connected with a reservoir or pressure vessel, *P*. If the reservoir be filled with a liquid, water for example, the latter under certain conditions will exert a downward pressure and act as a propelling or driving power, the degree of which will depend on the height of the column and may be represented by *H*. If the stopcock at *O* be opened the column of water, which has heretofore been exerting an equal pressure in all directions, will now show its downward pressure, and in consequence it will be driven into and through the horizontal tube and discharged from its free extremity with a definite velocity. At the same time the fluid will rise in each vertical tube to a height directly proportional to the distance of each tube from the free extremity. The velocity with which the fluid is discharged can be determined by measuring the quantity, q, discharged in a unit of time, (1 second) and dividing it by the area of the tube, πr^2; viz., $v = \frac{q}{\pi r^2}$. Inasmuch as the tube is of uniform diameter the velocity through each cross-section will be the same.

As the water flows through the horizontal tube it meets with resistance, namely, the cohesion and friction of its molecules, and the adhesion between the walls of the tube and the water which must be overcome if the flow is to continue. Because of the fact that water will moisten most surfaces with which it comes in contact there will be an adhesion between the walls of the tube and the outer layer of the column of water, in consequence of which it will become more or less retarded in its flow. Between the outer retarded layer and the axis of the stream, there is an infinite number of layers of molecules, the cohesion of which one for the other is more and more overcome by the pressure in the vessel, *P*. The force of adhesion between wall and fluid, together with the force of cohesion between the molecules of the fluid give rise to the resistance of the fluid to the flow.

As a result of the resistance the forward movement of the water under the pressure in *P*, is somewhat retarded, and as a consequence it will exert a lateral or radial pressure against the walls of the tube. That such a pressure exists is shown by the rise of the fluid in each of the vertical tubes, and the height to which it rises in each tube is a measure of the pressure at its base. In the tube *f*, the fluid rises to but a slight extent for the reason that the resistance yet to be overcome is slight in amount. It is, however, a measure of the resistance or friction between the base of the tube and the orifice of outflow. In the tube *e* the fluid rises twice as high as in *f* because of the additional friction between the bases of the tubes *e* and *f*. What is true of these two points is equally true of the points at the base of the tubes *d*, *c*, *b*, *a*. Lines drawn to the pressure vessel from the top of the fluid in each tube and parallel to the horizontal tube will show how much of the pressure force is utilized in overcoming the friction in each section of the horizontal tube. The amount of the lateral pressure at any given point is therefore indicated and measured by the height to which the water rises in the tubes. For this reason these tubes are termed pressure tubes or piezometers.

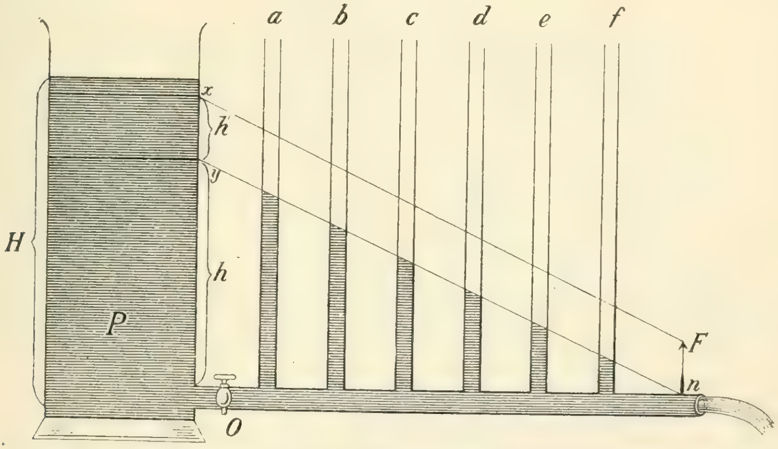

Fig. 151.—A Pressure Vessel, *P*, with a Horizontal Outflow Tube, *O–n*, into which Vertical Tubes or Manometers are Inserted.

Since the resistance in a tube of uniform diameter is proportional to its length the lateral pressure will gradually but progressively decrease from the reservoir to the outlet. Therefore the pressure at any given point is proportional to the resistance yet to be overcome and conversely the resistance to be overcome is indicated by the amount of the pressure. (In the conduct of an experiment the propelling power should be kept constant by permitting fluid to flow into the reservoir as rapidly as it flows out of the horizontal tube.)

The power or force which overcomes the resistance in the horizontal tube and imparts velocity to the fluid is the downward pressure of the water in the reservoir, represented by H. The amount of this power utilized in overcoming the resistance is approximately determined by drawing a line from the outlet to the reservoir, uniting the upper levels of the water in the vertical tubes. The height of the fluid at the point at which the line intersects the reservoir, y, is a measure, therefore, not only of the resistance but also an indication of the relative amount of the pressure used in overcoming it and is therefore known as the *pressure* height and indicated by the letter, h.

The amount of the pressure consumed in imparting the observed velocity is determined by ascertaining the height from which a particle must fall in empty space to acquire this velocity. This is obtained by dividing the square of the velocity by twice the accelerating force of gravity, 980 centimeters, as expressed in the formula, $\frac{v^2}{2g}$; the quotient is the height and is known as the velocity height. Conversely if the moving fluid were discharged into empty space through an opening in the tube at n, it would ascend an equal distance. If now this height is represented by F, and a line be drawn from it, parallel to the line of pressure until it meets the reservoir at x, it will be seen what percentage, $x\ y$, or h' of the primary propelling power is consumed in imparting the observed velocity.

Of the total pressure a small portion is left over which is utilized in forcing into, and overcoming the resistance offered by, the orifice of the horizontal tube. The initial pressure in P therefore divides itself mainly into two portions; one, the larger by far, h, is utilized in overcoming the resistance to the flow of the water; the other, the smaller, h' in imparting velocity.

Thus the two phenomena presented by the flow of a liquid through a tube with rigid walls and of uniform diameter are *velocity* and *pressure*, of which the former is the same for each cross-section, and the latter at any point directly proportional to the resistance to be overcome.

If, instead of a horizontal tube of uniform diameter, there be substituted a tube the middle third of which is enlarged, the conditions will be similar to the previous case until the fluid flows into the enlarged portion, when the velocity will diminish, being inversely proportional to the area of the cross-section. The resistance will be also diminished and therefore less of the pressure force or driving power will be consumed than in the first section of the tube, and as a result, the lateral pressure will fall less rapidly than in the first section. When the liquid flows into the narrow or third section, the primary velocity returns. Though the resistance again increases the amount to be overcome is small, and hence there is a rapid and steady fall of pressure.

On the contrary, if a tube be substituted the middle third of which is narrowed, the conditions will be similar to the previous cases until the liquid flows into the narrowed section, when at once the velocity increases and becomes inversely proportional to the area of the cross-section; the resistance being increased at the same time, there will be a rapid consumption of the pressure force and a steep fall of lateral pressure. On flowing into the third section, the velocity again diminishes and the pressure falls though more slowly to the end of the tube.

THE FLOW OF A LIQUID THROUGH A SERIES OF BRANCHING AND AGAIN UNITING TUBES WITH RIGID WALLS UNDER A STEADILY ACTING PRESSURE

In a system of this character, such as represented in Fig. 152, there must follow as a result of the repeated branchings, a progressive increase in the total sectional area of the collective tubes coincident with a progressive decrease in the sectional area of individual tubes in the section B C, while in the section C D, there must follow a progressive decrease in the total sectional area of the collective tubes coincident with a progressive increase in the sectional area of individual tubes, consequently there will be a combination of the two conditions alluded to in the two preceding paragraphs, namely, an enlargement of the stream bed coincident with a diminution in size of the individual tubes composing it, in the middle section. Moreover, for the purpose here intended it may be assumed that the tubes composing the middle section C are microscopic in size and that their total sectional area bears to the sectional area of tube A the ratio of 600 to 1.

If the system is connected with a pressure vessel, as in the preceding instance, and the stopcock is suddenly opened, the column of water will exert a downward pressure, and in consequence the water will be driven into and through the system with a definite velocity and pressure.

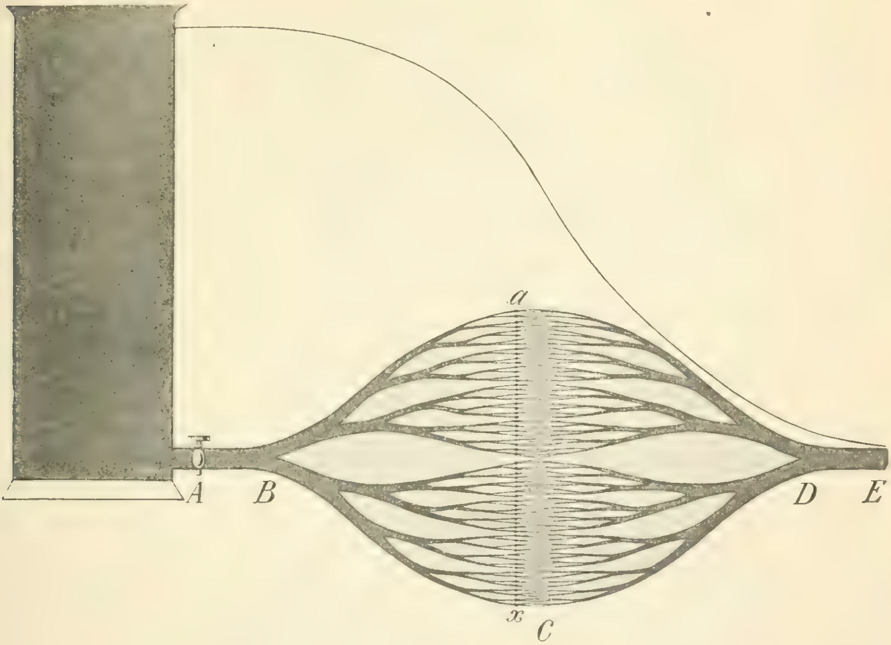

FIG. 152.—PRESSURE VESSEL WITH A SERIES OF PROGRESSIVELY BRANCHING AND AGAIN UNITING TUBES.

a, x, a series of stopcocks by which the peripheral resistance can be increased or decreased.

The *velocity* of the fluid will gradually decrease from B to C in a ratio inversely proportional to the total area of each cross-section until at C, it will attain its minimal value; the velocity will again increase from C to D in a ratio inversely proportional to the total area of each cross-section until at E, when it will attain the value it had in A if the entrance and exit tubes have the same area.

The *lateral pressure* will gradually fall from the beginning to the end of the system, though the fall must be more rapid in B–C than in A–B as will be clear from the following considerations.

In the section B–C the two factors—viz.: the widening of the stream bed which *decreases* the resistance, and the narrowing of the individual tubes which *increases* the resistance—exert an opposing influence on the pressure; hence the fall of pressure will be proportional to the ratio between these two factors. As the *increase* in the resistance due to the progressive decrease in the size of the individual tubes preponderates considerably over the *decrease* in the resistance due to the widening of the stream bed, there must be an increase in resistance in the area B–C and therefore a more rapid fall of pressure than in A–B. This fall, however, will not be as steep as it might be for the reason that the decrease in the velocity is attended by a decrease in the resistance and hence a lessened consumption of the propelling power. In the section C–D the two factors, viz.: the narrowing of the stream bed which *increases* the resistance, and the enlarging of the individual tubes which *decreases* the resistance, exert an opposing influence on the pressure, hence the fall of pressure will be proportional to the ratio between these two factors. As the *decrease* in the resistance due to the progressive enlargement of the individual tubes preponderates considerably over the *increase* in the resistance due to the narrowing of the stream bed, there should theoretically be a rapid fall of pressure from C to E. This rapid fall, however, will be to some extent prevented for the reason that the increase in velocity due to the narrowing of the stream bed increases the resistance to a high value and hence the pressure falls less rapidly than it otherwise would.

The pressure throughout the system is the result of (1) the downward pressure of the water in the reservoir, and (2) the resistance to its flow, due to the cohesion and friction of its molecules and its adhesion to the sides of the tubes, and its extent in any one section will be proportional to the resistance yet to be overcome. It will naturally be higher in the section A–B than in the section D–E, though the difference in the level of the pressure between these two points will not be as great as might theoretically be supposed from the small size of the tubes in C for the decrease in velocity counterbalances in part the resistance which they offer.

The general curve of the fall of pressure in this system is indicted by the curved line extending from the pressure vessel to the outlet of the horizontal tube.

The value of the pressures in these two sections and their relation to each other could be varied either temporarily or permanently by the insertion of a series of stopcocks a, x, along the course of the tubes between B and C in the neighborhood of their ultimate branchings by which an additional resistance could be superposed on the system from A to the stopcocks. If the lumen of each stopcock has a certain average value, so as to permit of a certain outflow of water, the pressure will have a certain value in both A–B and D–E. But if the lumen of each stopcock is decreased, there will be an increase in the resistance and hence a rise of pressure in A–B and a fall of pressure in D–E. If, on the contrary, the lumen of each stopcock is increased, there will be a decrease in the resistance and hence a fall of pressure in A–B and a rise of pressure in D–E. The stopcocks may be spoken of as a *variable peripheral resistance.*

In the foregoing exposition it has been assumed that in all instances the pressure in the pressure vessel was steadily acting. If, however, the pressure be made to act intermittently as it can be by alternately opening and closing the stopcock, at A both the velocity and the pressure will be alternately increased and decreased. The outflow of the fluid during the moment the pressure is acting will be rapid, and during the moment the pressure is not acting the outflow will cease. It becomes therefore intermittent. Coincidently there is an alternate temporary increase and decrease of the lateral pressure.

THE FLOW OF A LIQUID THROUGH A TUBE WITH ELASTIC WALLS UNDER AN INTERMITTENTLY ACTING PRESSURE

When a tube with elastic walls is connected with a pressure vessel, the conditions which are established on opening the stopcock and the consequent flow of water, will soon approximate those observed in a tube with rigid walls. As the water moves forward, it encounters friction, exerts a lateral pressure and causes a distention of the tube. This latter effect continues until the elastic recoil of the walls of the tube exactly counterbalances the pressure of the water from within. When this condition is established the tube becomes practically a tube with rigid walls, and hence so long as the primary pressure is uniform, the velocity and lateral pressure will obey the laws which hold true for rigid tubes.

If, however, the primary pressure be intermittently applied or alternately increased or decreased, and the water forced into the tube, previously filled with water but under no particular pressure, it will be forced out of the peripheral end of the tube more rapidly during the period of the increase of pressure and less rapidly during the period of the decrease of pressure or it may cease entirely. The extent to which the outflow becomes merely remittent, or entirely intermittent, will depend on the amount of resistance, whether this be due to length of tube or a narrowed outlet, and the degree of elasticity.

When these factors are of such a nature that the resistance is very high and the elasticity slight, the outflow will be intermittent. But if they are made to change gradually, and this is especially the case with the resistance, from a slight to a greater value, the outflow gradually changes from an intermittent to a remittent and finally to a continuous outflow and for the following reasons:

With a given resistance and elasticity, the fluid which is driven into the tube by the action of the primary pressure exerts more or less lateral pressure, gives rise to a distention of the tube, and acquires a certain velocity of outflow. In consequence of the distention, a portion of the fluid accumulates. With the cessation in the action of the primary pressure, the elastic walls recoil and force the accumulated fluid forward and so maintain more or less effectively the same velocity of outflow until there is a return of the pressure. If the resistance be great and the elasticity slight, this is impossible and the outflow will be entirely intermittent. But if they are made to increase in value, the proportionate amount of the fluid which accumulates during the action of the primary pressure will also increase in amount and hence there will be an increase in the distention of the tube. The elastic recoil will therefore be greater in amount and longer in duration, and hence the outflow will change to a remittent and finally to a continuous outflow.

Coincident with the action and cessation of action of the primary pressure there is a corresponding increase and decrease of the lateral pressure and when the intermittent action is sufficiently rapid, the excess of fluid entering the tube over that discharged becomes sufficiently great to maintain a certain average or mean pressure, which, however, undergoes an alternate increase and decrease with each variation in the primary pressure.

The temporary increase and decrease of the pressure and the consequent expansion and recoil of the tube in the neighborhood of the pressure vessel, give rise to a wave on the surface of the tube which is propagated with more or less rapidity—though with decreasing amplitude—from the beginning to the end of the tube and causing in each section a corresponding expansion and recoil, and which is known as the expansion wave.

If a system of branching and again uniting tubes with elastic walls arranged in a manner similar to that represented in Fig. 152 is connected with a reservoir, and the primary pressure is made to act intermittently, or is alternately increased or decreased, phenomena will be presented which closely resemble the phenomena presented by the circulatory apparatus at the time of the heart beat.

THE APPLICATION OF THE FOREGOING FACTS TO THE VASCULAR APPARATUS

The systemic vascular apparatus may be conceived of as a system of tubes which have symmetrically divided and subdivided and afterward again united and reunited in a corresponding manner. The arteries, arterioles, capillaries, venules, and veins may therefore be schematically arranged (Fig. 153) in a manner identical with the schematic arrangement of tubes represented on page 335. The heart, with which they are in connection, when filled with blood may be compared with the reservoir filled with water, and the intra-ventricular pressure developed during the contraction, to the downward pressure of the water when the stopcock at *A* is opened.

The Stream-bed.—The stream-bed, the path along which the blood flows, varies widely in its total sectional area in different parts of its course, being least in the aorta and venæ cavæ, and greatest in the capillaries. In passing from the base of the aorta toward the capillaries the sectional area of individual arteries, in consequence of repeated branching, diminishes, though their total sectional area increases and in direct proportion to their distance from the heart. In the capillary system the sectional area of an individual capillary attains its minimal value, though the total sectional area attains its maximal value. Comparing one with the other, it has been estimated that the total sectional area of the aortic bed is to the total sectional area of the capillary bed as 1 is to 600 or 800. This statement is based on the estimated values of the sectional area of the aorta, 615 mm., the velocity of the blood in the aorta 300 mm. per second, the average velocity in the capillaries 0.5 mm. per second. If these estimates are accepted as approximately correct, then the sectional area of the capillary system or bed is obtained by the following formula:

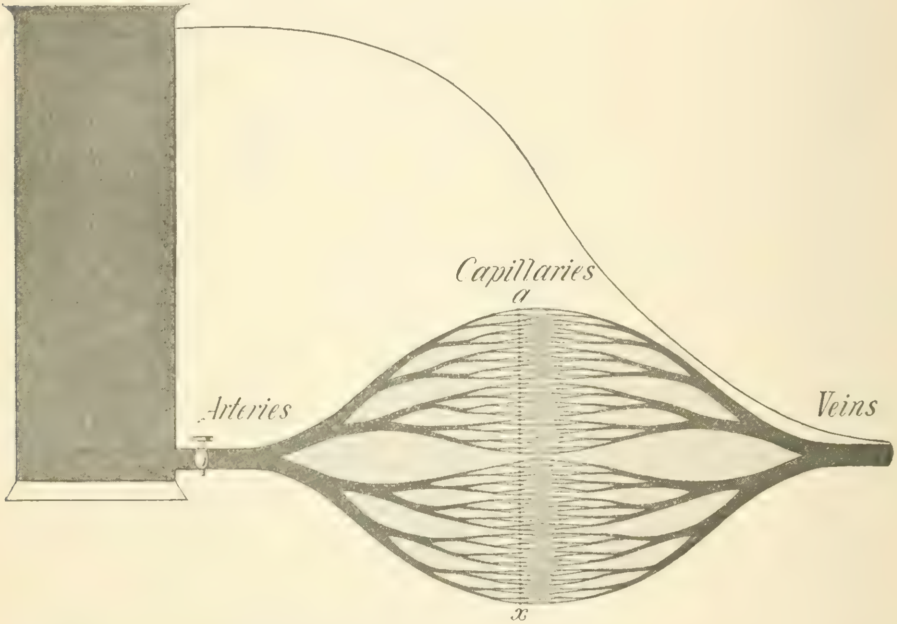

FIG. 153.—SCHEMATIC ARRANGEMENT OF THE VASCULAR APPARATUS.

a, *x*, the arteriole muscle by which the peripheral resistance can be increased or decreased.

$x = \frac{615 \times 300}{0.5}$ or 369,000 mm., a ratio of the aortic sectional area to the capillary sectional area of 1 to 600. In passing from the capillary into the venous system the sectional area of individual veins increases, though the total sectional area decreases and in direct proportion to their distance from the capillaries.

The stream-bed in the aorta is relatively narrow, but widens gradually as it approaches the capillaries, where it attains its maximal width; it again narrows gradually as it passes into the veins, until in the venæ cavæ it becomes almost as narrow as in the aorta. As the combined sectional areas of the venæ cavæ are greater than the sectional area of the aorta, the stream-bed of the former never becomes as narrow as that of the latter.

The gradual increase in the width of the stream-bed from the beginning of the aorta to the middle of the capillary system, and the gradual decrease in the width of the stream-bed from the middle of the capillary system to the terminations of the venæ cavæ, which result from the repeated branching and subsequent uniting, as well as its relative width in the arteries, capillaries, and veins, are shown graphically in Fig. 154.

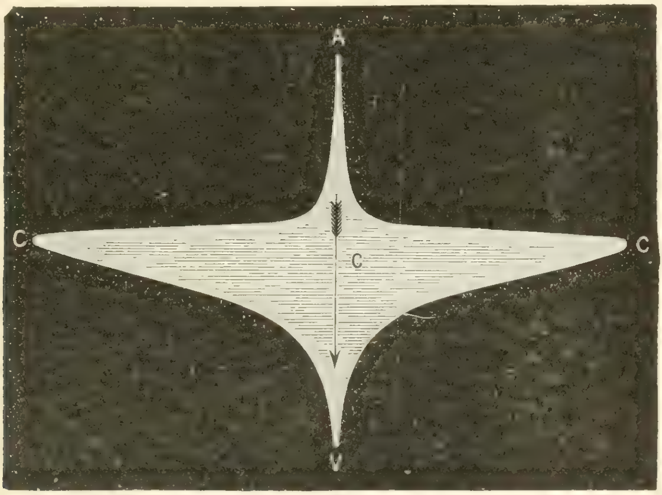

Fig. 154.—Diagram Designed to Give an Idea of the Aggregate Sectional Area of the Different Parts of the Vascular System. A. Aorta. C. Capillaries. V. Veins. The transverse measurement of the shaded part may be taken as the width of the various kinds of vessels, supposing them fused together.—(*Yeo.*)

The Intra-ventricular Pressure.—When the heart contracts and the intra-ventricular pressure rises above the pressure in the aorta, the aortic valves are suddenly forced open and the blood is driven into and through the arteries, capillaries, and veins to the right side of the heart and in accordance with foregoing considerations with a definite velocity and against a certain resistance, which in turn gives rise to a side pressure.

The Velocity.—The velocity of the blood in the systemic vascular apparatus will gradually decrease from the aorta to the middle of the capillary system in a ratio inversely proportional to the total area of any given cross-section of the stream-bed, until in the capillaries it will attain its minimal value, which is especially small because the resistance to the flow of blood in the capillaries increases inversely as the square of their diameters, while in the larger blood-vessels the increase is inversely proportional to the simple diameter; the velocity will again increase from the middle of the capillary system to the ends of the venæ cavæ in a ratio again proportional to the total area of each cross-section of the stream-bed until in the venæ cavæ it will attain its maximal value, though it will not attain its initial value in these vessels because their combined sectional area is greater than that of the aorta.

The Lateral Pressure.—The lateral pressure will also gradually fall from the beginning of the aorta to the ends of the venæ cavæ, though the fall will be most rapid at the periphery of the arteries. In the arterial system the fall of pressure will be proportional to the ratio between the *increase* in resistance due to the narrowing of individual vessels, and the *decrease* in resistance due to the widening of the stream-bed; as the former preponderates over the latter there must be an increase in resistance from the aorta to the capillaries and hence a sharper fall of pressure toward the termination of the arterioles, which is very steep for reasons to be stated later. In the venous system the fall of pressure will continue and its rate will be proportional to the ratio between the increase in resistance due to the narrowing of the stream-bed, and the decrease of resistance due to the enlarging of individual vessels; as the latter preponderates over the former there should be a rapid fall of pressure from the capillary system to the ends of the venæ cavæ. This, however, is to some extent prevented for the reason that the increase in velocity due to the narrowing of the stream-bed increases the resistance to a relatively high value and hence the pressure falls less rapidly than it otherwise would.

The Resistance.—The resistance to the flow of blood through the systemic vascular apparatus is due to the cohesion and friction of its molecules as well as that of the corpuscles and the adhesion of the blood to the sides of the vessels. The resistance is also increased by the small diameter of the capillary blood-vessels.

The high pressure characteristic of the arterial system contrasted with the low pressure characteristic of the venous system determined by experiment, cannot be accounted for alone by the resistance offered by the small diameter of the vessels of the capillary system. This in itself would be insufficient to maintain the observed differences in pressure in the different sections of the vascular apparatus necessary for physiologic purposes. To meet this necessity there has been developed at the periphery of the arterial system, in the arteriole wall, a special muscle, a, x, Fig. 152 which by contracting can add a *physiologic* resistance to what might be termed the *physical* resistance of the system. According to the degree of its contraction will the resistance to the flow of blood from the arteries to the veins at the periphery of the arterial system be increased and the arterial pressure be raised and the venous pressure be lowered. According to the degree of its relaxation will the resistance to the flow of blood from the arteries into the veins be decreased at the periphery of the arterial system and the arterial pressure be lowered and the venous pressure raised. By this means the extent and the relation of the pressure in the two main sections of the systemic vascular apparatus can be temporarily or permanently changed in one direction or the other. The effect of the diminution in the caliber of the arteriole due to the contraction of the muscle is spoken of as the *peripheral resistance.*

That the high pressure in the arteries is largely due to this physiologic factor is shown by the rapid and pronounced fall of pressure that occurs when this muscle suddenly relaxes as it does when the spinal cord is transversely divided in the cervical region, thus cutting off from the arteriole muscle those nerve influences that largely determine its contraction. Under such circumstances the pressure in the dog may fall from approximately 140 mm. to 40 mm. of mercury or even less. Stimulation of the distal extremity of the spinal cord will be followed by the temporary contraction of the arteriole muscle and a rise of pressure to its former value.

The Distribution of the Intra-ventricular Pressure.—The pressure developed during the ventricular contraction is thus expended in imparting velocity to the blood and overcoming the cohesion and friction of its molecules. The percentage of the pressure utilized in overcoming the resistance could be approximately determined from the pressure in the aorta if this were accurately known; the percentage of the pressure utilized in imparting velocity could be determined with the formula $\frac{v^2}{2g}$, if the actual velocity of the blood in the aorta could be experimentally determined. On account of the difficulty in obtaining this latter factor at least, the results must be only approximative.

An idea of the ratio between the velocity pressure and the resistance pressure, however, may be obtained from the distribution of the aortic pressure in the dog in reference to the carotid artery. Thus, if it be assumed that the average velocity of the blood is 35 cm., the velocity pressure is equal to $\frac{(35)^2}{1960}$ or 0.62 centimeters of blood or 0.046 centimeters of mercury, and if the average aortic pressure is 150 mm. of mercury, the ratio of the velocity pressure to the resistance pressure is as 1 to 326.

The Pulse Wave.—Inasmuch as the heart's action is intermittent and the walls of the arteries are elastic, there is a temporary increase and decrease of the pressure with each beat of the heart, attended by a corresponding expansion and recoil of the arteries, giving rise to a wave on the surface of the arteries which is propagated with more or less rapidity—though with decreasing amplitude—from the beginning of the aorta to the capillaries, and causing in each successive section a corresponding expansion and recoil, and which is known as the expansion wave or pulse wave.

The general statements regarding the phenomena attending the flow of blood through the systemic vascular apparatus contained in the foregoing paragraphs will be further elaborated in the following pages. For special reasons it is convenient to consider the pressure first.

BLOOD-PRESSURE

Blood-pressure may be defined as the pressure exerted radially or laterally by the moving blood-stream against the sides of the vessels. This pressure is the result of (1) the driving power of the heart, and (2) of the resistance offered to the forward movement of the blood—a resistance due to the cohesion and friction of the molecules of the blood, of the blood corpuscles, and the adhesion of the blood to the sides of the blood-vessels. That there is such a pressure within the arteries, capillaries, and veins, different in amount in each of these three divisions of the vascular apparatus, is evident from the results which follow division of an artery or a vein of corresponding size. When an artery is divided, the blood spurts from the opening for a considerable distance and with a certain velocity. The reason for this lies in the fact that the vessel has been distended by the pressure from within and its walls thrown into a condition of elastic tension, so that at the moment there is an outlet, the vessel suddenly recoils and forces the blood out with a velocity and to a height proportional to the distention. When a vein is divided, the blood as a rule merely wells out of the opening with but slight momentum, and for the reason that the vessel has been but slightly, if at all distended by the pressure. These results indicate that the blood in the arteries stands under a pressure considerably higher than that of the atmosphere, while that in the veins stands under a pressure perhaps but slightly above that of the atmosphere. Especially true is this of the larger veins.

The difference in the height of the pressure in the arterial system as contrasted with the venous system is due to the progressive diminution of the resistance from the beginning of the aorta to the ends of the venæ cavæ, together with the small diameter of the capillaries, increased to a variable extent, by the tonic contraction of the arteriole muscle.

The same facts may be demonstrated in another and more striking way. A dog or cat is anesthetized and securely fastened in an appropriate holder. The carotid artery on the right side and the jugular vein on the left side are freely exposed and clamped. Into the artery there is inserted on the distal side of the clamp and in the direction of the heart a cannula to which is connected a tall glass tube, 200 cm. high and of about 4 mm. internal diameter. Into the vein there is passed on the proximal side of the clamp and in the direction of the capillaries a second cannula, to which is connected a similar tube, though of less height. If the two clamps are removed at the same time, the blood will mount in both tubes simultaneously. In the arterial tube the blood will ascend by leaps corresponding to the heart-beats until a certain height is reached, when the column becomes relatively stationary, being kept in equilibrium by the blood-pressure within the vessel and the atmospheric pressure without. Though stationary in a general sense, nevertheless the blood-column oscillates, rising and falling with each contraction and relaxation of the heart. Not infrequently larger excursions of the column are seen which correspond in a general way to the respiratory movements. This experiment was originally performed on the horse, by the Rev. Stephen Hales (1732).

In the venous tube the blood also rises to a certain height, after which it remains quite stationary, as the effect of the cardiac contraction is not propagated under normal conditions beyond the arterial system. The height to which it rises is but slight as compared with that in the arterial tube. The pressure in both vessels is thus recorded in millimeters of blood. Strictly speaking the pressure thus obtained does not represent the *lateral* pressure in the carotid artery but in the vessel from which it arises. The central end of the carotid is, under the circumstances, but a continuation of the cannula and the pressure thus obtained is the lateral pressure of either the innominate artery or the aorta as the case may be. In order to obtain the lateral pressure in the carotid or any other artery it is only necessary to take the end pressure of any one of its branches or what amounts to the same thing, to divide the vessel and insert the horizontal portion of a **T**-shaped tube into the central and distal ends through which the blood can continue to flow, and to connect the vertical portion with a vertical pressure tube or with a mercurial manometer. The absolute pressure on any given unit of vessel surface—*e.g.*, 1 sq. mm.—is obtained by multiplying the height of the column, expressed in millimeters, by the unit of surface, and then determining the weight of this mass of blood. Thus if the height of the column of blood in the carotid artery tube is 2000 mm., then the pressure on 1 sq. mm. is the weight of 2000 mm. of blood. The weight of 2000 c.mm. of blood is equal to 2.1 grams.

The Arterial Blood-pressure.—For accurate and long-continued observation the arterial blood-pressure is more conveniently studied by means of a **U**-shaped tube (a manometer) partially filled with mercury. One limb of the manometer is connected by means of a tube and a cannula with an artery (Fig. 155). For the purpose of retarding coagulation of the blood and for preventing the escape of a large volume of blood from the vessels, the system is filled with a solution of carbonate of soda of sp. gr. 1060, 55.8 grams per 1000 c.c., or a 25 per cent. solution of magnesium sulphate of sp. gr. 1060, and under a pressure approximately equal to that in the vessel of the animal as determined in previous experiments. When communication is established between the vessel and the cannula, the mercurial column adjusts itself to the pressure in the artery and at once exhibits the same cardiac oscillations and respiratory undulations as did the column of blood in the previous experiment.

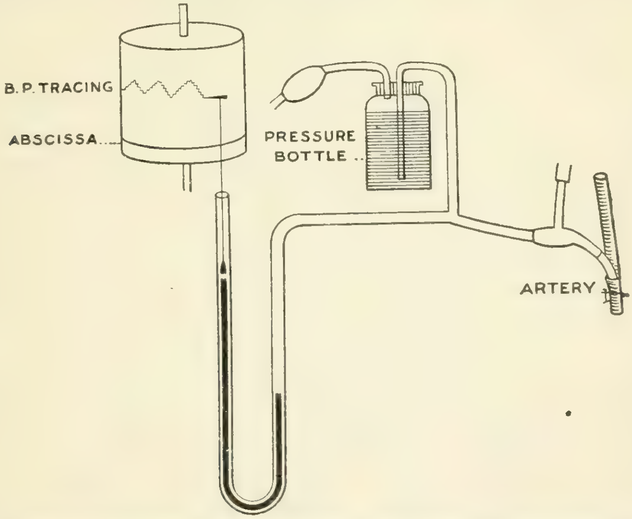

FIG. 155.—DIAGRAM TO SHOW THE RELATION OF THE MERCURIAL MANOMETER TO THE ARTERY, ON ONE HAND, AND TO THE RECORDING CYLINDER, ON THE OTHER HAND, WHEN ARRANGED FOR RECORDING BLOOD-PRESSURE.

The height of the mercurial column kept in equilibrium by the pressure of the blood within, and the pressure of air without the vessel is that between the lower level of the mercury in the proximal, and the higher level in the distal limb of the manometer, both of which can be read off on a scale placed between the two limbs.

The height of the mercury as well as its oscillations in the distal limb may be recorded by placing on the top of the mercury a light float, the upper end of which carries a writing point. When the latter is placed in contact with the moving blackened surface of a recording cylinder or kymograph, the height and the oscillations are recorded in the form of a tracing similar to that shown in Figs. 155 and 156, in which the smaller oscillations represent the changes in pressure due to the systole and diastole of the heart and the larger oscillations to variations in the average pressure due to the respiratory movements. The height of the mercurial column kept in equilibrium at any particular moment is determined by measuring the distance between a base-line or abscissa, which represents the position of the mercury at atmospheric pressure, and any given point on the trace above, and multiplying it by 2, for the reason that the mercury sinks in the proximal limb as high as it rises in the distal limb of the manometer and hence the column of mercury supported is that observed between the upper and lower levels of the mercury in the distal and proximal limbs of the manometer.

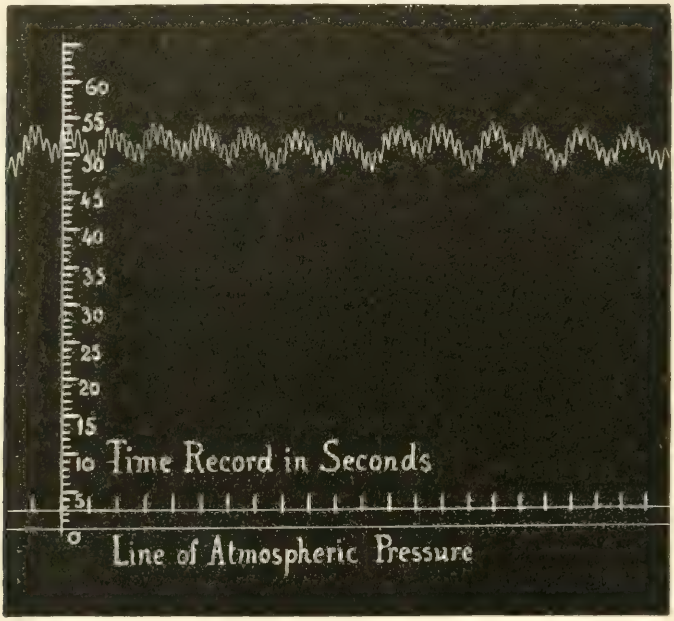

FIG. 156.—A PORTION OF A BLOOD-PRESSURE TRACING OBTAINED FROM THE CAROTID ARTERY OF THE RABBIT WITH A MERCURIAL MANOMETER. The small oscillations are due to the heart-beat; the large oscillations are due to the respiratory movements.

The blood-pressure as revealed by the tracing may be resolved into two components: viz., (1) a more or less constant element represented by the pressure in the arteries during the period of the cardiac diastole, which is termed the diastolic or minimum pressure; and (2) a variable element represented with certain limitations by that additional pressure occurring at the time of the cardiac systole, which is termed the systolic or maximum pressure. The diastolic pressure is represented by the distance between the base-line and the points of the curve corresponding to the diastolic pause; the systolic pressure, by the distance between the base-line and the apices of the curves following the cardiac systole. The relation of these two components varies in different animals and in the same animal at different times. If the diastolic pressure is low, the systolic increase may be considerable; if the former is high, the latter may be slight in extent.

There are good reasons for believing, however, that this record does not represent either the true diastolic or the true systolic pressure but that the limits between the two are far more widely apart than here represented. For, owing to its inertia, the mercury is not capable of following the rapid variations of the pressure throughout their extent, that occur with each heart-beat. The employment of one of the various forms of the quickly responsive spring manometers such as are used in determining the rapid variations of intra-cardiac pressure will show a much greater difference between the diastolic and systolic pressures, often amounting to as much as 40 millimeters.

For the purpose of obtaining the maximum systolic and the minimum diastolic pressures, it is best, however, to insert between the cannula and the manometer a maximum and a minimum valve similar in principle to that shown in Fig. 157. By permitting the blood to exert its pressure first through the maximum valve and then permitting the mercurial column to exert its pressure through the minimum valve in the reverse direction for a certain length of time, the maximum systolic and the minimum diastolic pressures will be recorded. By this method Dawson found an average maximum systolic pressure in the carotid artery of the dog of 162, and a minimum diastolic pressure of 103 mm. of mercury, a difference of 59 mm. Hg. The difference between these two pressures is known as the *pulse* pressure. (A diagram showing the relation of these different pressures one to another will be found on page 348.)

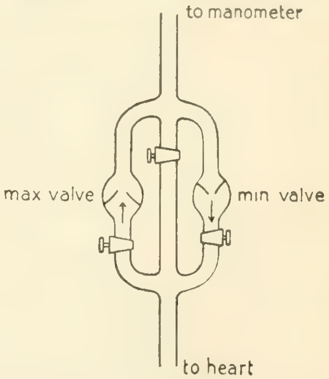

FIG. 157.—V. FRANK'S VALVE. This is placed in the course of the tube between heart and manometer, so that the latter may be used as a maximum, minimum, or ordinary manometer according to the tap which is left open.—(*Starling.*)

In a series of experiments it will be found that the blood-pressure in the arteries, recorded with the mercurial manometer, though rising and falling a certain number of millimeters, yet retains a fairly constant general average, the result of an adjustment between the number of heart-beats per minute and the amount of the resistance offered to the escape of blood into the capillaries and veins. Though the tracing fails to record accurately the diastolic and systolic pressures it approximates a certain *average* or *mean* of the pressure thus recorded, which represents the power driving the blood through the vessels. It is frequently stated that in a tracing in which the respiratory undulations are absent, the mean pressure is the arithmetic mean of the systolic and diastolic pressures. This is, however, not strictly correct, for if the pressure is recorded by means of a spring manometer or a sphygmograph applied over the artery of man, a record much different in appearance and similar to that shown in Fig. 158 will be obtained. In such a record it will be observed that the passage from the lowest diastolic pressure (*a*) to the highest systolic pressure (*b*) takes place quickly, occupying about 0.1 second; and that the change from the highest systolic pressure to the succeeding lowest diastolic pressure takes place slowly, in about 0.7 second, and that the line of descent is interrupted by a secondary rise and fall of pressure before the former diastolic level is reached.[1] If a horizontal line is drawn across the record parallel to a line uniting the lowest diastolic levels, and to a line uniting the highest systolic levels and in the position of the arithmetic mean, the triangular record of the pressure changes will be divided into two portions of which the upper has a smaller area than the lower portion from which it is apparent that the pressure is low for a longer period that it is high and hence the mean pressure cannot be the arithmetic mean between the diastolic and systolic pressures. The mean pressure, however, can for a given period at least be experimentally determined. Thus, if at some one point between the artery and the manometer, the lumen of the connecting tube be largely obliterated by a constriction, the variations in the pressure following the systole and diastole of the heart will be largely, if not entirely excluded, and the mercury, instead of rising rapidly in the manometer and fluctuating with each heart-beat, will rise slowly to a certain level and then remain at rest. The number of millimeters of mercury thus supported represents the *mean* or absolute pressure. The same result can be obtained by employing the compensatory manometer of Marey which presents a constriction of this character. From many experiments made by Dawson it has been learned that the mean pressure lies nearer to the diastolic than to the systolic pressure and may be expressed numerically by the statement that it is equal in millimeters of mercury to the diastolic pressure plus one-third of the pulse pressure. In a tracing in which the respiratory undulations are present the mean pressure can be calculated. The method by which this is done, however, is rather complicated and need not be detailed here. In a general way the mean pressure in such a tracing may be represented by a line drawn horizontally across the tracing midway between the apex and trough of the undulation.

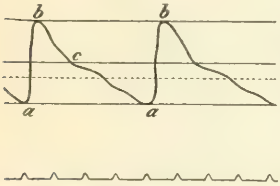

FIG. 158.—Sphygmogram or pulse curve.

Estimates of the Mean Arterial Pressure.—Because of the difficulty in obtaining the pressure in small arteries, the experimental determinations have for the most part been confined to large arteries such as the carotid, brachial, and femoral, and hence the results which have been obtained have reference to the lateral pressure in the aorta or in the large vessels which immediately arise from it. The pressure obtained in the usual way at the central end of a divided carotid is generally known as the "end pressure" and represents the mean lateral pressure in the aorta or in the innominate artery. Among the results thus obtained in different experiments from the carotid artery of different animals are the following: In the horse, from 122 to 214 mm. Hg.; in the dog, from 140 to 160 mm.; in the cat, 150 mm.; in the rabbit, from 90 to 100 mm.; in the sheep, 170 mm.; in the calf, from

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[1] It must be remembered, however, that the cardiac systole endures though with diminishing energy, even though the systolic pressure in the artery is falling, for 0.32 second, when a rapid dilatation sets in attended by the closure of the semilunar valves, an event indicated in the tracing by the notch preceding the second rise of pressure at c.

133 to 165 mm. In two observations made on human beings previous to the amputation of a limb, the pressure was found in the brachial artery of one patient to vary from 110 mm. to 120 mm. Hg., and in the anterior tibial artery of the other patient from 110 mm. to 160 mm. Hg.

The investigations made in different parts of the arterial system indicate that the mean pressure is remarkably constant and uniform and does not show any noticeable falling off until near the arteriole region where the resistance suddenly and rapidly increases. Thus Volkman found simultaneously in the carotid artery and in the metatarsal artery of the sheep a mean pressure of 165 and 146 mm. Hg. respectively and this for the reason that the resistance throughout the arterial system does not markedly increase until the arteriole region is reached. The careful investigations of Dawson show that in the large blood-vessels of the dog the diastolic pressure is as constant as the mean pressure though it undergoes slight variations in different regions; but that the systolic pressure, as shown by taking the end pressure in the thyroid and similar sized arteries in different parts of the arterial tree, undergoes a considerable falling off, though it, too, remains high in large arteries.

The numerical expressions of these various pressures in different parts of the arterial system are shown in the following table abstracted from the more extensive tables of Dawson. The results were obtained from experiments made on dogs. The figures represent in millimeters of mercury certain average end pressures in the arteries named.

Artery	Systolic	Mean	Diastolic	Pulse pressure
Brachio-cephalic	163	121	103	60
Right carotid	160	118	110	50
Left carotid	160	123	101	59
Left subclavian	168	123	105	63
Left brachial	160	118	110	50
Left renal	165	123	103	62
Deep femoral	152	118	102	50
Thyroid	140	118	97	43

The Capillary Pressure.—The small size of the capillaries precludes an investigation of their pressure by manometric methods. It may be stated, however, to be approximately equal to the pressure required to obliterate their lumina and to whiten the skin. The apparatus of v. Kries is based on this theory. A small glass plate, from 2.5 to 5 sq. mm., is fastened to the under surface of a support of suitable size carrying a small scale pan. The glass plate is placed on the skin near the root of a finger-nail and the scale pan gradually weighted until the vessels are obliterated, as shown by the blanching of the skin. From results obtained with this apparatus v. Kries estimated the pressure in the capillaries of the hand at 37 mm. Hg. and in the ear at 20 mm.

The Venous Pressure.—In passing from the capillaries to the heart the pressure continues to fall. The increasing size of the veins permits again of manometric observations in different regions. In the crural vein the pressure has been found to be equal to 14 mm. Hg., and in the brachial vein 9 mm. of Hg. In the jugular and subclavian and other vessels near the heart it is zero or even *negative;* that is, less than atmospheric pressure to the extent of from 1 to 10 mm. of mercury.

The amount and relation of the different pressures in the three divisions of the systemic vascular apparatus are approximately shown in Fig. 159.

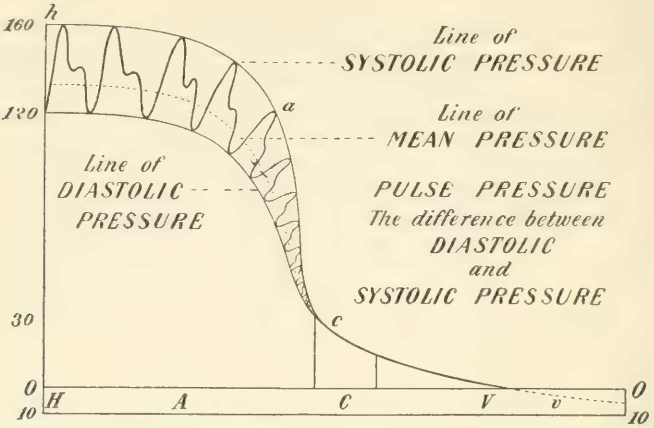
160
h
120
30
0
10
Line of SYSTOLIC PRESSURE
a
Line of MEAN PRESSURE
Line of DIASTOLIC PRESSURE
PULSE PRESSURE The difference between DIASTOLIC and SYSTOLIC PRESSURE
c
H
A
C
V
v
0
10

FIG. 159.—A DIAGRAM DESIGNED TO SHOW THE AMOUNT AND THE RELATION OF THE BLOOD-PRESSURE IN THE THREE DIVISIONS OF THE VASCULAR APPARATUS, AS WELL AS THE RELATION OF THE DIASTOLIC, THE MEAN, AND THE SYSTOLIC PRESSURES IN THE ARTERIAL SYSTEM. Based on experiments made on dogs. H. Heart. A. Arteries. C. Capillaries. V. Large veins. O, O, being the zero line (=atmospheric pressure), the pressure is indicated by the height of the curve. The numbers on the left give the pressure (approximately) in millimeters of mercury. *h.* Pressure in heart. *a.* Arteriole region showing sudden fall of pressure. *c.* The fall of pressure in the capllaries. *v.* The negative pressure in the large veins.

RÉSUMÉ OF THE FACTS OF THE BLOOD PRESSURE AND OF THE FACTORS WHICH CAUSE IT

From a consideration of the foregoing facts and statements the following résumé may be made: 1. The blood during its flow exerts a pressure against the sides of the blood-vessels. 2. This pressure is the resultant on the one hand of the intra-ventricular pressure developed at the time of the contraction, and on the other hand of the resistance to the forward movement of the blood. 3. The resistance is to be sought for in the cohesion and friction of the molecules of the blood and its adhesion to the walls of the vessels. 4. The resistance is inversely proportional to the diameter of the vessel and is therefore least in the large arteries and veins and greatest in the arterioles and capillaries. 5. The pressure is highest in the aorta where it may amount in man to 150 mm. of mercury above that of the atmosphere, and lowest at the ends of the venæ cavæ where it may be no greater than that of the atmosphere or may be even 10 mm. Hg. below it. 6. The pressure falls from the beginning to the end of the vascular apparatus, though not progressively, for throughout the large vessels of the arterial system it continues relatively high. 7. The high pressure in the aorta is due to the total resistance of the vascular apparatus and the pressure at any given point of the apparatus represents the resistance yet to be overcome. 8. The high pressure in the arterial system and its marked fall at the periphery is more especially the result of the very great resistance at this point, known as the *peripheral* *resistance*, the result of a rapid diminution in the diameter of the arterioles and the capillary vessels, together with the tonic contraction of the arteriole muscle. 9. The pressure in the arterial system undergoes considerable variation both above and below the mean pressure during the systole and diastole of the heart.

The Heart.—The primary factor in the production of the pressure is the pumping action of the heart. Should there be any cessation in its activity, the elastic walls of the arteries would recoil and force the blood into the veins. There would be coincidently a fall of the pressure to that of the atmosphere. Even under normal circumstances this condition is approximated during the diastole. The recoil of the arterial wall by which the forward movement of the blood is maintained is attended by a fall in pressure. But before this reaches any considerable extent, the heart again contracts and forces its contained volume of blood into the arteries.

That this may be accomplished it is essential that the cardiac energy be sufficient not only to drive a portion of the blood through the capillaries into the veins, but to oppose the recoiling arteries, and to distend them to their previous extent, so that the incoming volume of blood may be accommodated. This at once reëstablishes the pressure at its former level.

During the contraction of the heart the kinetic energy is transformed into potential energy, represented by the tense distended walls of the arteries. With the relaxation of the heart and the closure of the semilunar valves the potential energy of the arteries is again transformed into kinetic energy, represented by the moving blood. The artery thus continues the work of the heart during its period of inactivity. The rapidity with which the cardiac contractions succeed each other prevents the pressure from sinking below a certain average level.

The Resistance.—The secondary factor is the resistance to the flow of blood through the vessels, the nature of which has been previously stated. So long as the resistance, and especially that variable element of it at the periphery of the arterial system, maintains a certain average value, so long will the pressure in each division of the vascular apparatus maintain an average or a physiologic value. Should the resistance at the periphery of the arterial system vary in either direction, the result of an increase or a decrease in the degree of the contraction of the arteriole muscle, there will arise a change in the relative degree of pressure in each of the three divisions of the vascular apparatus.

The Elasticity of the Vessel Walls.—A tertiary factor is the elasticity of the arterial wall. While it can hardly be said that the elasticity is a cause of the pressure, there can be attributed to it the capability of modifying and assisting in the maintenance of the pressure at a more or less constant level; for were it not for this property of the vessel wall the variations in pressure during and after the systole would be far more extensive than they are, and would approximate the variations observed in tubes with rigid walls. The elasticity, moreover, assists in the equalization of the bloodstream, converting the intermittent and remittent flow characteristic of the large arteries into the continuous equable stream characteristic of the capillaries. It also permits of wide variations in the amount of blood the arteries can contain between their minimum and maximum distention.

VARIATIONS IN THE BLOOD-PRESSURE

A. In the Arterial Pressure.—It is apparent from the preceding statements that the arterial blood-pressure as a whole may be increased above the normal, by:

1. An *increase* in the rate or force of the heart's contraction.
2. An *increase* in the peripheral resistance.
3. An *increase* in both the force of the heart and the peripheral resistance;

and it is further apparent that if the pressure is *higher* than the normal it may be lowered to the normal by a decrease in either one or both of these factors.

It is also apparent that the arterial blood-pressure as a whole may be decreased below the normal by:

1. A *decrease* in the rate and force of the heart's contraction.
2. A *decrease* in the peripheral resistance.
3. A *decrease* in both the force of the heart and the peripheral resistance;

and it is again further apparent, that if the pressure is *lower* than the normal it may be raised to the normal by an increase in either one or both of these factors.

1. If when the arterial pressure is in a condition of equilibrium the heart ejects into the arteries in a given period of time an increased quantity of blood as a result of an increased rate of contraction, there will be an accumulation of blood temporarily in the arteries and a rise of pressure (the peripheral resistance remaining the same), for the reason that the pressure is only sufficient to force into the capillaries a given volume, in the same period of time. As the pressure rises the velocity and the outflow will be increased until equilibrium is restored though at a somewhat higher level. A rise of pressure from an increase in the rate of the beat alone has been questioned, for it has apparently been demonstrated that there is a definite relation between the normal rate and the volume discharged from the ventricle, and that when the rate is increased, the volume discharged diminishes and hence the pressure remains normal or even falls below the normal. Nevertheless, if the inhibition of the heart be lessened, or entirely removed, as by division of one or both vagi, there is generally a rise in the blood-pressure coincident with the increased cardiac rate.

An increase in the pressure is readily brought about by an increase in the force or power of the contraction, the frequency remaining the same. An increase in the volume of blood ejected at each contraction will necessarily lead to an accumulation. With the accumulation there goes an increased distention of the artery and a corresponding increase of pressure. In a short time, therefore, the increased pressure will force out of the arteries at a higher rate of speed this excess of blood until the outflow again equals the inflow. This restores the equilibrium but establishes the mean pressure at a higher level.

2. If the peripheral resistance is increased by a contraction of the muscle walls of the arterioles, the frequency and force of the heart remaining the same, there will also be an accumulation of blood in the arteries, an increased distention and consequent rise of pressure. The outflow of blood will at the same time be diminished.

Arteriole contraction and a consequent rise of blood-pressure may be experimentally brought about by an increase in the activity of the general vaso-motor center due to the arrival of nerve impulses transmitted to it through certain afferent nerves as when after division of the sciatic nerve in a curarized animal the central end is stimulated with induced electric currents (Fig. 160), or by injecting into the blood, adrenalin, which it is generally believed acts on the muscle fibers of the vessel walls. Fig. 161 Physiologic causes may act in the same way and reflexly cause arteriole contraction. A rise of pressure from this cause much beyond the normal is to a large extent prevented under physiologic conditions by a simultaneous *decrease in the rate and force of the heart-beat.* This is due to a stimulation of the peripheral ends of the depressor nerve, and a consequent reflex stimulation of the cardio-inhibitor center, and not to a direct action on the heart-muscle, inasmuch as the effect is not observed after division of the vagi.

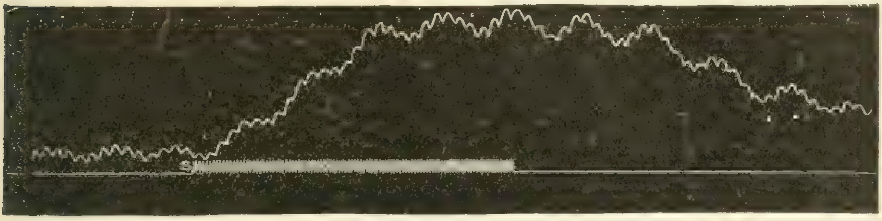

FIG. 160.—A TRACING SHOWING AN INCREASE IN THE BLOOD-PRESSURE IN THE CAROTID ARTERY OF A RABBIT DUE TO AN INCREASE IN THE PERIPHERAL RESISTANCE FROM A CONTRACTION OF THE ARTERIOLES CAUSED BY REFLEX STIMULATION OF THE VASO-MOTOR CENTER. The nerve stimulated was the sciatic. Stimulation began at S. The rate of the heart-beat is unchanged. With the cessation of the stimulation the blood-pressure falls for the reverse reasons.

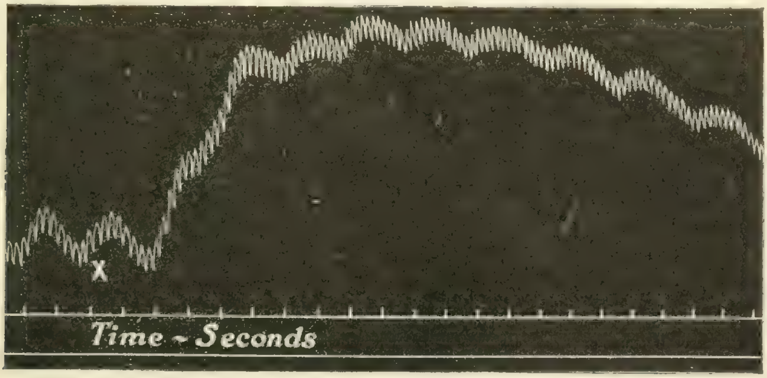

FIG. 161.—TRACING SHOWING THE RISE OF BLOOD PRESSURE IN A CAT after the intravenous injection of minute doses of adrenalin injection at x. The abscissa should be 40 millimeters lower.

3. When both the force of the heart and the peripheral resistance are simultaneously increased there is a rapid increase in pressure, the former factor tends to increase, the latter factor, to decrease, the velocity of the outflow. According as the one or the other preponderates, will there be an increase or decrease in velocity. If they balance each other, there will be

no change. A rise of pressure from a combination of these factors is rather a pathologic than a physiologic condition and is observed in certain diseases of the vascular apparatus.

The converse of these statements also holds true.

1. If when the general arterial pressure is in a condition of equilibrium the heart ejects into the arteries in a given period of time a lessened quantity of blood, either as a result of a decrease in the rate or force, there will soon be a diminution of the arterial distention and a consequent fall in pressure. The velocity at the same time diminishes. This continues until the outflow no longer exceeds the inflow. Equilibrium will again be established, but the pressure will be at a lower level.

The decrease in the rate and force of the heart may be brought about suddenly or more or less gradually by direct stimulation of the inhibitor fibers in the trunk of the vagus nerve with strong or with weak electric currents respectively (Fig. 162); or, by a stimulation of the cardio-inhibitor center by nerve impulses transmitted to it through certain afferent nerves, *e.g.*, the afferent fibers in the vagus, when stimulated with induced electric currents (Fig. 163).

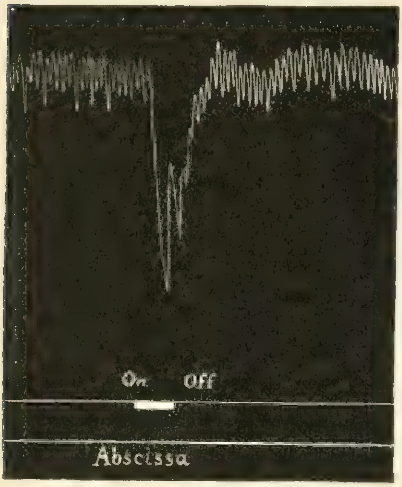

Fig. 162.—A Tracing of the Blood-pressure in the Carotid Artery of a Rabbit, showing a sudden decrease in the pressure due to an arrest in the rate and force of the heart-beat the result of stimulating the vagus nerve from "on" to "off." With the cessation of the stimulation the pressure began to rise as the rate and the force of the heart-beat returned. (The abscissa should be 20 mm. lower.)

2. If the peripheral resistance is diminished by a dilatation of the arterioles, the heart's contractions remaining the same, the outflow of blood at once increases and the existing pressure soon diminishes.

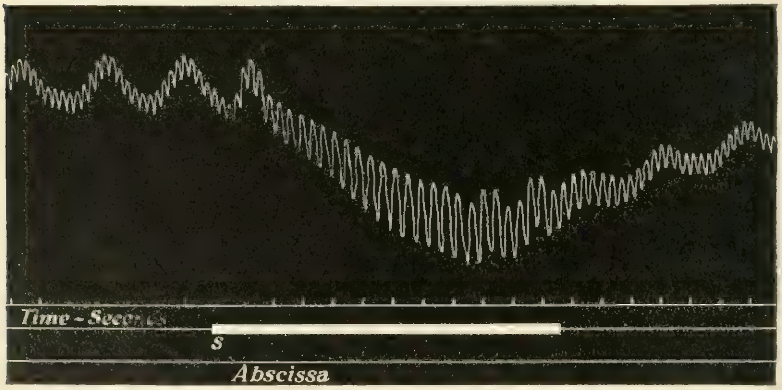

Fig. 163.—Tracing Showing Reflex Inhibition of the Heart and Fall of Blood-pressure in the Cat, following stimulation of the central end of the vagus nerve.

As a rule a diminution in peripheral resistance is attended by *an increase* *in the rate or force of the heart*, and this is especially the case if the pressure has been above the normal.

The decrease in the peripheral resistance, *i.e.*, in the arteriole contraction and its effect on the blood-pressure may be brought by a depression or inhibition of the activity of the general vaso-motor center due to the arrival of nerve impulses transmitted to it by certain afferent nerves, *e.g.*, the depressor nerve (see page 386), when, after division, its central end is stimulated; or by the inhalation of amyl nitrite, which it is generally believed, acts locally on the muscle walls of the arterioles and causes their relaxation (Fig. 164).

3. When both the force of the heart and the peripheral resistance are simultaneously diminished, there will be a rapid fall in pressure. The former factor tends to decrease, the latter factor to increase the velocity of outflow.

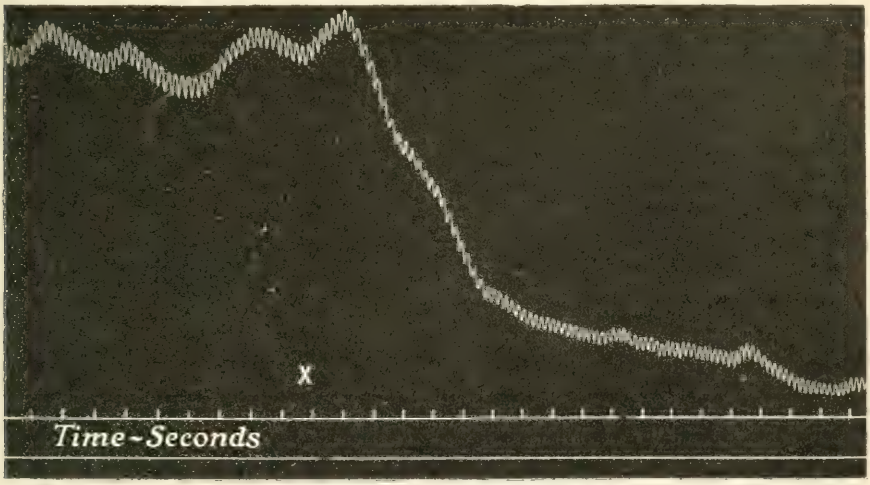

FIG. 164.—TRACING SHOWING THE FALL OF BLOOD-PRESSURE IN THE CAT, following the inhalation of amyl nitrite. Inhalation begun at X.

According as the one or the other preponderates will there be a decrease or an increase in velocity. If they balance each other there will be no change. This condition is also a pathologic rather than a physiologic condition and observed in states of profound depression due to serious injuries.

Local Variations in the Arterial Blood-supply.—The variations in pressure and velocity from variations either in the activity of the heart or in the peripheral resistance recorded in preceding paragraphs, have reference to the arterial system in its entirety; but it is evident from many facts that similar variations take place in special regions or organs of the body. Thus, it is a well-known fact that for the exhibition of the functional activity of every organ there must be an increase in the volume of blood supplied to it in each unit of time. This is accomplished by an active dilatation of the arterioles of the artery of supply, and unless the area or organ supplied is large, as the splanchnic area for example, there will be no necessary diminution in either the general blood-pressure or the average velocity. With the cessation of functional activity, there is no longer any need for so large a blood-supply and hence the arterioles contract, diminish the outflow, and raise the pressure. If, on the other hand, the area to be supplied be large, as the splanchnic area, the dilatation of the intestinal arteries will be attended by such a large inflow of blood that not only will there be a fall of pressure in these vessels, but a fall of pressure in other arteries as well, combined with a diminution in velocity through them. With the contraction of the intestinal arteries the reverse conditions at once arise. By constant variations in the peripheral resistance of individual arteries in each and every region of the body, and in association with variations in the rate or force of the heart, the blood is shunted now into this, now into that organ in accordance with its functional needs. All variations in peripheral resistance are largely brought about reflexly by the vaso-motor nerves, the origin, distribution, and mode of action of which will be considered in subsequent paragraphs.

B. In Capillary Pressure.—The pressure in the capillaries, though for the most part possessing a permanent value, is subject to variations in accordance with variations in the pressure in either the arterial or venous systems or both. The marked difference in the pressure in the large arteries and the capillaries is partly due to the resistance offered by the narrow arterioles. If the latter dilate in any given area, the capillary pressure increases because of the propagation into them of the arterial pressure. The reverse condition would decrease the pressure. On the other hand, any interference with the outflow from any given area, due to venous compression, would likewise increase the pressure; any factor which would, on the contrary, favor the outflow would decrease the pressure. Independent of any change in the arteriole resistance, it is evident that a rise in arterial pressure alone would increase the capillary pressure. If both arterial and venous pressures rise, the capillary pressure increases; if both fall, it decreases.

C. In Venous Pressure.—Independent of any change in the venous pressure in a given area from local or temporarily acting causes—*e.g.*, aspiration of the thorax or heart, muscle contractions, change of position, etc.—the general venous pressure will be *increased* by a decrease in the value of those factors which produce the difference of pressure between the arteries and veins. An increase in the value of these factors would necessarily *decrease* the pressure.

Variations in the Relation of the Arterial and Venous Pressures.—So long as the heart maintains a given rate and force and the resistance at the periphery of the arterial system (due to the contraction of the arteriole muscle) a given value, will the usual physiologic difference between the pressure in the arteries and veins remain unchanged. If, however, either factor changes in one direction or another, there will arise a change in the relative degree of pressure in the different divisions of the vascular apparatus. Thus if the heart force increases and a larger volume of blood is discharged into the arteries in a unit of time, the amount of blood in the venous system diminishes, and the result is a rise of the arterial and a fall of the venous pressures. If, on the contrary, the heart force decreases or the mitral valve permits of a regurgitation, a smaller volume of blood is ejected into the arteries in a unit of time, the amount of blood in the venous system increases, and the result is a fall of the arterial and a rise of the venous pressure.

Again if the arteriole muscle relaxes and a larger volume of blood flows from the arteries into the veins in a unit of time, the result will be a fall of arterial and a rise of venous pressure. If, on the contrary, the arterial muscle contracts and a smaller volume of blood flows into the veins, the reverse change of pressure obtains.

The Determination of the Arterial Blood-pressure in Man.—Inasmuch as the blood-pressure undergoes considerable variation in both physiologic and pathologic conditions as well as in response to the action of drugs, it seemed desirable to possess some means by which an accurate knowledge of the pressure under a variety of conditions could be obtained both for diagnostic and therapeutic purposes. The foregoing method of obtaining the blood-pressure not being of general application to human beings for obvious reasons, special instruments have been devised by which the pressures may be determined at least approximately without resorting to any surgical procedure.

By reason of the fact that both the systolic and diastolic pressures are regarded as important factors in clinical conditions, and their determination of value for diagnostic and therapeutic purposes in diseases of the circulatory apparatus, it is desirable to have clear ideas of what is meant by these terms. If the changes of pressure are registered by a sphygmograph, a curve resembling that shown in Fig. 173, page 367, will be recorded, which shows more or less accurately the qualitative, if not the quantitative variations, of the pressure in the arteries during a cardiac cycle.

Systolic pressure may be defined as the highest pressure developed in the artery during the systole of the heart and occurs in the first half of the systole and is therefore of very short duration; after this the pressure begins to fall, but endures until the close of the systole, indicated in this curve by the notch preceding the elevation *c*.

Diastolic pressure may be defined as the lowest pressure in the artery during the diastole of the heart and occurs at the end of the diastolic period just before the time of the succeeding systole. The diastolic pressure gradually falls from the time of closure of the semilunar valves to the end of the diastolic period.

The instruments by which these pressures are determined are called *sphygmomanometers*. Some of the many forms of this instrument are adapted for obtaining the systolic pressure only, while others are adapted for obtaining either the systolic or the diastolic pressure, or both.

The principle involved in the first group is the application of a hydrostatic pressure to an artery, *e.g.*, the temporal, radial, etc., until the lumen is completely obliterated as indicated by the disappearance of the pulse beyond the point of compression, and at the same time the registration of the pressure applied, by means of a mercurial or spring manometer. The pressure just sufficient to obliterate the pulse or to allow it to reappear after obliteration, is taken as the systolic pressure.

The principle involved in the second group is based on a suggestion of Marey, that the maximum pulsation of the artery or the maximum distention and recoil following a heart-beat would be most likely to take place when an elastic pressure applied to the outside of an artery is just sufficient to equalize the diastolic pressure within. Inasmuch as these pulsations can be transmitted to, taken up and reproduced by a mercurial column in connection with the pressure appliances, it becomes possible, when the maximum oscillation of the mercurial column is attained, to read off the diastolic pressure.

The truth of this suggestion was subsequently demonstrated by Howell and Brush. These experimenters connected the right carotid artery of a dog with a mercurial manometer, interposing along the course of the connecting tube a maximum and a minimum valve. The left carotid artery was surrounded by a plethysmograph which was connected, with both a mercurial and a spring manometer, the former for the purpose of indicating the pressure necessary to obtain the greatest oscillation, the latter for the purpose of magnifying and recording the pulsation. When the observations were simultaneously made it was found that the diastolic pressure in the right carotid measured by the minimum manometer was almost exactly equal to the pressure measured by the manometer in connection with the sphygmomanometer surrounding the left carotid artery, when it was exhibiting its maximum excursions. The difference in the results of the two sides scarcely exceeded more than one or two millimerers of mercury. It was, therefore, established that the greatest oscillations record diastolic pressure.

Many forms of sphygmomanometers adapted for clinic purposes, with which both the systolic and the diastolic pressures can be obtained, have been devised. With all forms however, the pressure is applied to the arm by a rubber armlet which is at least 8 centimeters wide. This is the widest armlet that can be adjusted to the average-sized arm and presents distinct advantages over narrower armlets. This armlet is prevented from expanding outward by a cuff composed of some unyielding material held in position by straps which completely encircle the cuff. The rubber armlet is connected by stiff-walled rubber tubes with a mercurial manometer on the one hand and with a rubber bulb or air piston on the other hand. In using the apparatus the pressure is raised by forcing air into the closed system—distending the rubber armlet and with the same degree of force—changing the levels of the mercury in the manometer, until the pulse is no longer felt at the wrist. By special devices the pressure is then carefully lowered until the mercurial column begins to fall. At a given level it exhibits a considerable oscillation which may be mistaken for the actual systolic pressure but which is probably due to the impact of the blood against the upper edge of the rubber portion of the cuff. If the column of mercury be still further lowered so that the pressure indicated is a trifle lower than the systolic pressure the blood will be forced through the compressed artery and give rise to a pulse wave, which may be felt at the wrist. The highest excursion of the mercurial column noted by the eye at the moment the pulse reappears is regarded as the *systolic* pressure.

The pressure is then lowered 5 millimeters at a time and the oscillations of the mercurial column noted. As the pressure is thus slowly lowered there will come a moment when the oscillations will attain a maximum value and beyond which the oscillations again diminish. The lowest level of the mercury column at the time of the sudden termination of the greatest oscillation is taken as the *diastolic* pressure.

Erlanger's sphygmomanometer is a most valuable instrument for obtaining both systolic and diastolic pressure. It possesses an advantage in that it is provided, in addition to the mercurial manometer, with a tambour and lever by which changes in pressure can also be recorded on a revolving cylinder (Fig. 165). A complete description of this apparatus, the manner of using it and the results that can be obtained with it will be found in the Johns Hopkins Hospital Reports, Vol. XII.

With this apparatus, the lever often exhibits a considerable oscillation even when the pressure exerted on the arm exceeds the systolic pressure. It is difficult, therefore, to determine at times the moment at which the pressure indicated by the mercurial column just falls below the systolic pressure and allows the blood to pass through. A new criterion for this determination has been furnished by Erlanger. With a given speed of the drum, the up and down strokes of the lever practically coincide. But if the speed of the drum be slightly increased "so that each wave subtends about 1½ to 2 mm. of smoked paper (this speed is attained merely by removing the governor), the change

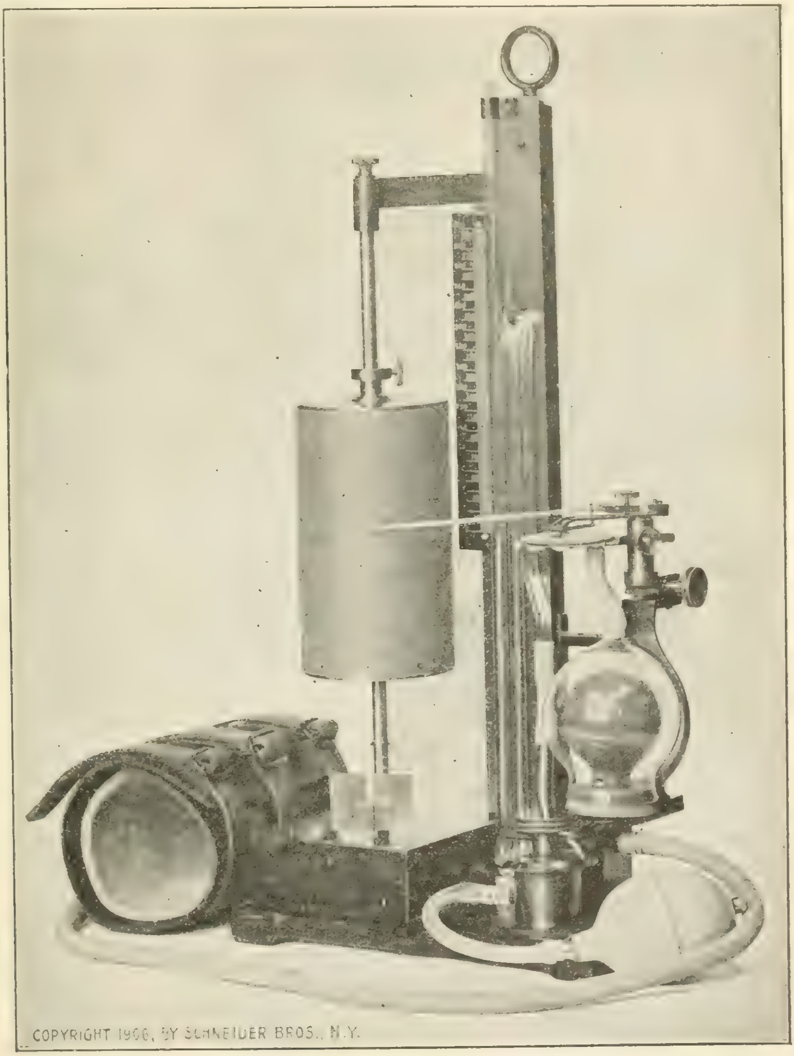

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Fig. 165.—Erlanger's Sphygmomanometer.

in form of the successive waves manifests itself usually as a more or less abrupt separation of the ascending and descending strokes of the pulse record (Fig. 166). The phenomenon may vary somewhat with the form of the pulse wave and may even be obscured by fling, but there has been no great difficulty in recognizing it in every case. It is often very clear when the tracing shows no abrupt increase in amplitude whatsoever. It is just as accurate an index to the systolic pressure as the 'sensory criterion' and that of v. Recklinghausen. The change in form occurs because, at the moment the pressure on the artery falls below systolic, blood succeeds in making its way beneath the cuff. This must be squeezed out before the lever can return to the base line, whereas at higher pressures the lever is raised only through the hydraulic ram action of the pulse wave upon the upper edge of the cuff."

The conclusions of Erlanger regarding the results of his investigations with this apparatus may be partially summed up in the following statements, and as they hold true for other forms of apparatus which determine both systolic and diastolic pressures, they are here appended: "The pressure that is determined by occluding an artery is probably the maximum end pressure of the artery occluded. The pressure determined by the method of maximal oscillations is the minimum lateral pressure of the artery compressed, and, therefore, as the minimum lateral pressure is the same in all of the larger arteries, the *pulse pressure*, determined when the pressures in the brachial artery are observed, tends to approximate the lateral *pulse pressure* in the aorta."

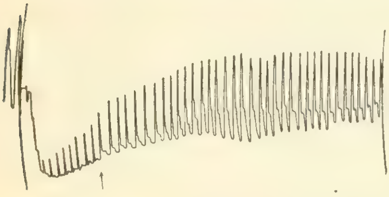

FIG. 166.—TRACING SHOWING THE POINT, INDICATED BY THE ARROW, AT WHICH THE SYSTOLIC PRESSURE IS TO BE NOTED.—(*Erlanger.*)

Any positive statement as to the numerical values of the different pressures is somewhat difficult to make inasmuch as they will vary within physiological limits in accordance with the position of the body, exercise, character of psychic states, digestion, temperature, and other conditions. For comparative investigations it is necessary, therefore, to place the subject of the investigation in one and the same position, to apply the cuff to the corresponding arm, to use always a uniform width of cuff and to select the same time of day with reference to meals, etc.

It may be stated, however, that in adult life the systolic pressure in the brachial artery ranges from 110 to 135 millimeters of Hg. in men and about 10 mm. less in women; the diastolic pressure ranges from 65 to 110 mm. Hg.; the pulse pressure ranges from 25 to 40 mm. Hg.

The Auscultatory Method of Determining the Blood-pressure.—In 1905 a new method was introduced and described by Korotkow for the determination of both the systolic and diastolic pressures, which in the experience of clinicians is more accurate and satisfactory in both physiologic and pathologic conditions than any of the other clinical methods. (See papers by Goodman and Howell in the Univ. of Pa. Medical Bulletin, Nov., 1910 and the American Journal of the Medical Sciences, September, 1911). It consists in the interpretation of certain sounds heard with the stethoscope, in the artery under observation when it is gradually released from a pressure that has obliterated its lumen in a given region.

In the employment of this method the brachial artery is selected and compressed in the usual manner with a wide cuff in connection with a graduated mercurial manometer.

After the pulse has been obliterated the stethoscope is placed over the artery below the cuff, care being taken to prevent undue pressure. On releasing the pressure in the cuff very gradually as in the employment of other methods a series of sounds corresponding with each arterial pulsation is heard as the pressure falls from the systolic to the diastolic level. The series of events are spoken of as phases of which five are recognized.

The first phase is characterized by a loud clear-cut snapping sound: the second phase is characterized by a series of murmurs; the third phase by a succession of loud clear snapping sounds which resemble very closely those of the first phase but are less loud; the fourth phase is inaugurated by a sudden decrease in the intensity of the murmurs of the third phase giving rise to what is described as a dull tone that rapidly becomes weaker and soon fades away; the fifth phase is one of silence.

These phases which are sharply defined and easily distinguishable are believed to be associated with vibrations of the arterial walls. The first sound is generally believed to be due to the sudden distention of the artery, by the inrush of blood beneath the cuff, and indicates the systolic pressure which can be at once observed by the height of the mercury in the manometer. This sound lasts until the pressure falls about 14 millimeters. The second sound, a succession of murmurs, is believed to be caused by whirlpool eddies in the blood stream as it is propelled from the partially constricted artery into the non-constricted region below the cuff. These murmurs last until the pressure falls about 20 millimeters. The third sound is attributed to the vibration of the arterial wall but as the lumen of the artery is so much greater than that of the compressed portion the rapidity of the current is less and hence the sound is neither so sharp nor pronounced. It lasts until the pressure falls about 6 millimeters. The transition from the second to the third sound involves a fall of about 5 millimeters. The disappearance of the sounds is coincident with the return of the artery to its normal size and hence a cessation of the vibration. It therefore indicates the diastolic pressure, which can at once be observed by the height of the mercury in the manometer.

The systolic pressure obtained by this method corresponds to the first sound that is heard over the brachial artery and is about 130 millimeters; the diastolic pressure corresponds with the cessation of all sounds and is about 85 millimeters.[1] The pulse pressure is therefore 45 millimeters.

In pathologic states of the vascular apparatus the duration and intensity of the sounds undergo considerable modification. In some diseases they are quite characteristic and hence have both a diagnostic and therapeutic value.

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[1] The statement that the fifth phase is the index of minimum pressure is in dispute. Weysse and Lutz, using the Erlanger sphygmomanometer for comparison with the auscultatory phenomena, have shown that the onset of the fourth phase occurs as the oscillations recorded by the sphygmomanometer begin to decrease in amplitude and, therefore, this phase rather than the fifth phase should be taken as index of minimum pressure.

THE VELOCITY OF THE BLOOD

From the number of heart-beats per minute, 72, and the amount of blood discharged from the left ventricle at each beat, 80 c.c., it is evident that the blood must be flowing through the vascular apparatus with a certain velocity, for during the minute the entire volume of blood, 3684 grams, must have passed one and a half times through the heart. Direct observation of the escape of blood from the central end of a divided artery, and from the peripheral end of a divided vein, as well as of the flow through the capillaries as seen with the microscope, shows that the velocity of the flow varies in different parts of the vascular apparatus. In the arteries, moreover, the flow is not quite uniform, but experiences an alternate acceleration and retardation with each heart-beat. In the capillaries and veins the flow is continuous and uniform, as the conditions of the arterial walls are such as to completely overcome the intermittency.

If the systemic vascular apparatus be conceived of as a system of tubes which have symmetrically divided and subdivided, and have again united and reunited in a corresponding manner, it is clear that the total sectional area will steadily increase from the beginning to the middle of the system, and then as steadily decrease from the middle to the end of the system. In such a system the same volume of blood must pass through any given section in a unit of time if the balance of the circulation is to be maintained. As the velocity of a fluid is inversely as the sectional area of the tubes through which it flows, it follows that the initial mean velocity of the blood in the aorta will steadily decrease as it flows into the steadily enlarging stream-bed until it reaches a minimal value in the middle of the capillary system; and that it will again steadily increase as it flows into the narrowing stream-bed until it reaches the heart. The initial mean velocity of the blood in the aorta will not be attained in the venæ cavæ, for the reason that the total sectional area of the latter is somewhat greater than that of the former. The same facts hold true for the pulmonic vascular system.

The Mean Velocity in the Aorta.—From the well-known fact that the velocity with which a fluid is flowing through a tube may be determined by dividing its sectional area into the quantity discharged in a unit of time, attempts have been made to determine the mean velocity of the blood at the beginning of the aorta. If it be assumed that the volume discharged at each contraction is 80 c.c., and the number of heart-beats per minute is 72, the total volume discharged per minute would be 5760 c.c., or 96 c.c. per second. The sectional area of the aorta at its origin is 6.15 sq. cm. On the principle above stated, these two factors would show a velocity of 156 mm. per second. This being the case the velocity in the aortic arch at least would be considerably less than in the carotid artery as will be stated later, a fact which may however be explained on the assumption that owing to the curvature of the aorta and the extensibility of its walls the lateral pressure becomes very great; as a result the sectional area is increased and the velocity diminished. With the cessation of the heart's activity, the elastic recoil gives an impetus to the blood and increases its velocity.

The Mean Velocity in the Arteries.—The mean velocity of the blood in the larger and more superficially lying arteries has been determined by Volkmann with the hemodromometer, by Ludwig and Dogiel with the Stromuhr, and by other investigators with different forms of apparatus.

Since neither the blood nor any particle placed in it can be seen through the walls of the artery, it occurred to Volkmann to intercalate along the course of a vessel a **U**-shaped glass tube about one meter in length with a lumen the diameter of that of the selected vessel, into and through which the blood could be made to flow. The mechanic construction of the apparatus is such (Fig. 167) that the blood can be made to flow directly into the distal portion of the artery across the base or indirectly by way of the glass tube. Previous to the intercalation of the tube it is filled with serum or normal saline solution. With the turning of the cocks as B the blood enters the glass tube and drives the serum ahead of it into the arterial system. From the difference in time between the moment the blood enters and the moment it leaves the tube and from the capacity of the tube the velocity is determined.

The Stromuhr or rheometer of Ludwig (Fig. 168) is constructed on the same principle, but instead of the glass tube having the same diameter it is considerably enlarged on its two sides. The bulbs are fastened to a metallic disc which rotates around an axis in the metallic base which carries the tubes to be inserted into the arteries. With this device it is possible to place either bulb in connection with the proximal end of the artery. Previous to the

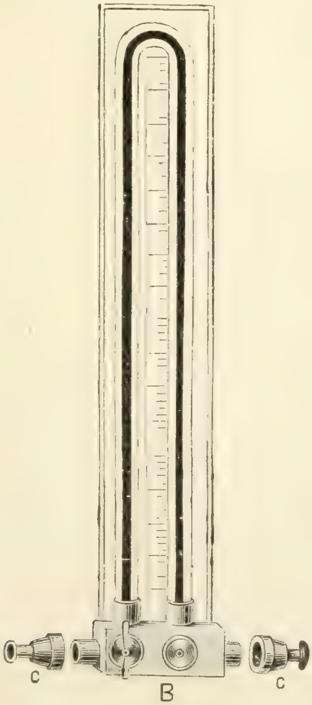

FIG. 167.—VOLKMANN'S HEMODROMOMETER. C, C. Arterial cannulas.

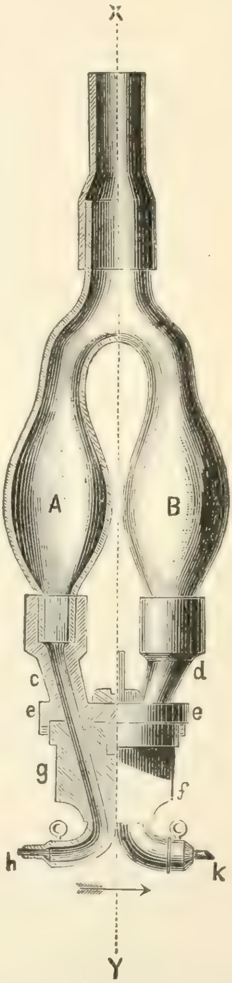

FIG. 168.—LUDWIG AND DOGIEL'S RHEOMETER. X, Y. Axis of rotation. A, B. Glass bulbs. *h*, *k*. Cannulas inserted in the divided artery. *e*, e_1, rotates on *g*, *f*. *c*, *d*. Tubes.

experiment the proximal bulb is filled with oil, the distal bulb with serum or normal saline. On removing the clips on the artery the blood flows into the proximal bulb and drives the oil into the distal bulb. As soon as the former is filled with blood the bulbs are reversed and the same relative conditions are attained. This is repeated a number of times. Knowing the capacity of the bulbs, and the number of times they are filled in a given period, the total quantity of blood discharged is obtained. This divided by the sectional area of the artery gives the velocity. The following values have thus been obtained: For the carotid of the dog, 205 to 357 mm. per second; for the carotid of the horse, 306 mm.; for the metatarsal artery of the horse, 56 mm. (Volkmann). For the carotid of rabbits, 94 to 226 mm.; for the carotid of the dog, 349 to 733 mm. (Dogiel).

The *variations* in the velocity of the blood in the arteries during the different phases of the cardiac cycle have been determined by Chauveau and Lortet with the hematachometer (Fig. 169). This consists of a metallic tube carrying a graduated disc. At one point the tube is perforated but covered with a rubber band through which passes an index. When the tube is inserted into the divided ends of an artery, the current of blood strikes the short arm of the index and gives to the outer long arm a movement in the opposite direction. The extent of the excursion indicates the velocity. The apparatus is first graduated with currents of water of known velocity. With this instrument Chauveau found that in the horse the velocity during the systole was 520 mm. per second, at the beginning of the diastole 220 mm. per second, and during the pause 150 mm. per second.

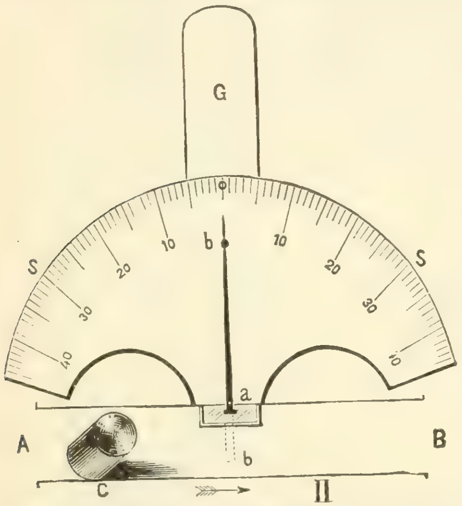

Fig. 169.—The Hemodromograph of Chauveau and Lortet. A, B. Tube inserted in artery. C. Lateral tube connected with a manometer. *b*. Index moving in a caoutchouc membrane, *a*. G. Handle.

The Velocity in the Capillaries.—The rate of flow in the capillary vessels cannot be experimentally determined. It has been estimated by Vierordt at 0.5 mm. per second in his own retinal capillaries; by Weber at 0.8 mm. In frogs the velocity can be fairly well determined by observing the time required for a corpuscle to pass over one or more divisions of an ocular micrometer. Weber calculated in this way that the velocity is 0.5 mm. per second.

As the velocity varies inversely with the sectional area, it becomes possible to approximately determine the relation of the sectional area of the capillary system to that of the aorta from the above-mentioned velocities. If it be assumed that the velocity in the aorta averages 300 mm. and in the capillaries 0.5 mm. per second, then the sectional area of the capillaries is to that of the aorta as 600 to 1.

The Velocity in the Veins.—In the venous system the velocity increases in proportion as the sectional area decreases. In the jugular vein Volkmann found the velocity 225 mm. per second, which was about one-half that in the aorta of the same animal. The reason for the slow rate of movement in the jugular vein is to be found in the fact that the sectional area of the combined venæ cavæ is about twice that of the aorta; hence the relation of the sectional area of the capillary system to the sectional area of the venæ cavæ is about 300 to 1.

The blood-pressure, the velocity of the blood, the sectional area of the vascular apparatus, and their relation one to the other are shown in Fig. 170.

The Relations of Blood-pressure and Velocity.—Though the pressure of the blood bears a definite relation to the velocity it must be kept in mind that it is rather the *difference in pressure* between the beginning and the termination of the arterial system, rather than the *mean* pressure that influences the velocity. Thus, with a given force of the heart and a given peripheral resistance, the velocity will have a given value, and so long as these factors remain constant will the velocity remain constant, even though the mean pressure should fall, as from a hemorrhage, or should rise, as from an injection of some indifferent fluid.

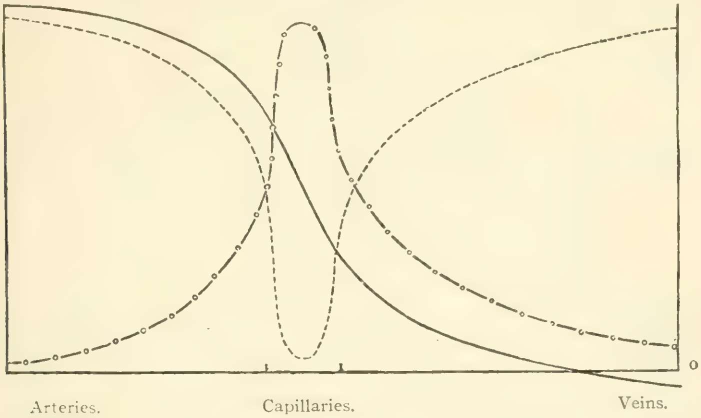

FIG. 170.— ———, Blood-pressure. -----, Velocity. —o—o—o—o, Sectional area.

If, however, the primary factors, viz.: the cardiac force or the peripheral resistance, change their values in either the same or opposite directions, there will be a change at once in the velocity. The variations in pressure and velocity, both in the same and opposite directions, which are theoretically possible from a change in the force of the heart, or in the peripheral resistance or both, are shown in the following table arranged by Waller. The plus sign indicates increase, the minus sign, decrease, in effect.

The statements herein embodied have been established by Marey with an artificial schema of the circulatory apparatus, and by Chauveau and Lortet by experiments on animals with the hemodromograph, a specially devised apparatus for this purpose.

Though all the relations between pressure and velocity in the table are possible, those which are most physiological are probably 5 and 6, for in both instances there is a minimum alteration in pressure, but a maximum alteration in blood flow or velocity. The first instance is the condition most favorable for the functional activity of organs, for the reason that the volume of blood which the organ receives in a unit of time is increased without any change in pressure; and it is an established fact that within physiological limits it is the volume of blood which an organ receives rather than the pressure under which it is received, that determines its activity. In the second instance, on the cessation of activity the velocity is decreased and the normal condition restored without any appreciable change in pressure.

No.	Heart	Arterioles	Blood-pressure	Blood flow
1	Force constant......	Resistance increased...	+	−
2	Force constant......	Resistance diminished.	−	+
3	Force increased	Resistance constant....	+	+
4	Force diminished...	Resistance constant....	−	−
5	*Force increased......*	*Resistance diminished..*	+ −	+ +
6	*Force diminished....*	*Resistance increased....*	− +	− −
7	Force increased.....	Resistance increased...	+ +	+ −
8	Force diminished...	Resistance diminished.	− −	− +

THE PULSE

The Arterial Pulse.—The pulse may be defined as a periodic expansion and recoil of the walls of the arterial system. The expansion is caused by the discharge from the heart into the arteries of a volume of blood, approximately 80 c.c., during the systole; the recoil is due to the elastic reaction of the arterial walls on the blood, driving it forward, into, and through the capillaries, during the diastole.

At the close of the cardiac diastole the arterial system is full of blood and considerably distended. During the occurrence of the succeeding systole, a definite volume of blood is again discharged into the aorta. The incoming volume of blood is now accommodated by the discharge of a portion of the general blood volume into the capillaries and by the expansion of the arteries both in a transverse and longitudinal direction. The expansion naturally begins at the root of the aorta and at the beginning of the systole. As the blood continues to be discharged from the heart, the expansion increases in extent; at the same time adjoining segments of the aorta and its branches expand in quick succession, and by the time the systole is completed the expansion has traveled over the entire arterial system as far as the capillaries. With the cessation of the systole and perhaps even before, the recoil of the arterial walls at once occurs, beginning at the root of the aorta and rapidly passing over the arteries to the capillaries.

The mode of development as well as the propagation of the expansion and recoil movement of the arterial wall, which together constitute the pulse, are illustrated in Fig. 171 in which A B represent the artery subdivided into six equal parts indicated by the letters *a* to *g*. In accordance with this subdivision of the artery the systole of the heart may be also divided into six parts, during the first three of which the heart increases in power, and during the last three of which it decreases in power, gradually falling to zero. The effect on the arterial wall of the discharge of blood from the ventricle is illustrated in the figure. During the first one-sixth of the systole a certain volume of blood is forced into the artery, which at this moment is already full of blood. Of this volume a portion moves forward while another portion moves sideways as the arterial wall begins to expand under the pressure of the heart. At the end of the first one-sixth of the systole the condition of the arterial wall may be represented by the lines 1*b*. During the second one-sixth the artery expands still more as the volume of blood increases under the increasing force of the heart, so that at the end of the second period the expansion of the arterial wall is not only greater at the point *a* but in addition has extended over a greater length of the artery so that the condition of the artery may be represented by the lines 2*c*. During the third sixth the same process continues; the incoming volume of blood still further expands the artery at *a*, as well as successive portions further on as far as *d*, so that at the height of the systolic power the condition of the artery may be represented by the lines 3*d*.

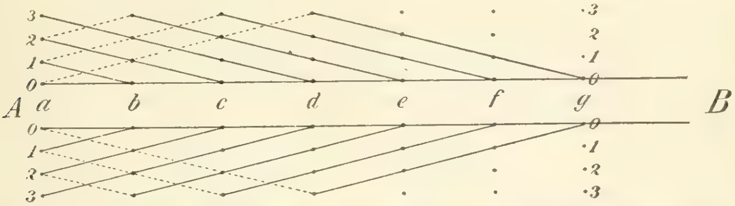

FIG. 171.—DIAGRAM SHOWING THE DEVELOPMENT OF A PULSE WAVE. (*Rollet.*)

The force of the heart now begins to decline and from this moment on, the elastic force of the artery preponderates and in consequence the arterial wall begins to recoil at the point *a*. At the end of the fourth sixth of the systole, therefore, the arterial wall at *a*, has recoiled to 2, while the expansion at *a* has advanced to *b*3 where the present force of the heart plus the elastic recoil of the arterial wall at *a*, are equal to the elastic force of the arterial wall at *b*. At this moment the condition of the artery may be represented by the lines 2, *b*3, *e*. During the two remaining sixths of the cardiac systole, the same process continues until, through elastic recoil, the artery has returned to its original condition at *a*, and the expansion has extended as far as *g*, while the height of the expansion has advanced to *d*3 where the force of the systole and the force of the elastic recoil balance each other. At the end of the systole the condition of the arterial wall may be represented by the lines *a*, *d*3, *g*, which indicates that the expansion and recoil of the artery, which together constitute the pulse, partake of the form of a wave the length of which is represented by the line *o*, *o*, and the height by the distance *d*3.

This expansion and recoil which thus pass from the beginning to the end of the arterial system assumes the form of a wave and therefore is known as the *pulse-wave* or *pulse*. Preceding and causing the expansion of the arterial system there is an increase of the general blood-pressure; preceding and leading to the recoil of the arterial system, there is a decrease of the general blood-pressure, both of which facts are shown by the small curves on a blood-pressure tracing, and for this reason the pressure which causes the expansion and recoil is termed the *pulse pressure*. It is defined as the rhythmic change in pressure at any given point of the arterial system; and in amount, is the difference between the diastolic and the systolic pressures, at the corresponding points. The volume of blood ejected from the ventricle is frequently termed the *pulse volume.*

The Velocity of Propagation of the Pulse-wave.—The propagation of the pulse-wave from its origin at the root of the aorta to any given point of the arterial system occupies an appreciable period of time. The difference in time between the systole and the appearance of the pulse-wave at the dorsal artery of the foot can be appreciated by the sense of touch. The absolute time occupied by the wave in reaching this point was determined by Czermak to be 0.193 second. The rate at which the wave is propagated over the vessels of the lower extremity has been estimated by the same observer at 11.16 meters per second, and for the upper extremities at but 6.7 meters per second. Other experimenters have obtained for the lower extremities somewhat different results, varying from 6.5 to 11 meters per second. Weber's original estimate was from 7.92 to 9.24 meters per second. The slower rate of movement in the vessels of the upper extremities has been attributed to a greater distensibility of their walls, a condition unfavorable to rapid propagation. For this reason a low arterial pressure will occasion a delay in the appearance of the pulse-wave in any portion of the body; a high arterial pressure will of course have the opposite effect. The difference in the speed of the pulse-wave and the blood-current shows that they are not identical and must not be confounded with each other.

The pulse-wave which thus spreads itself over the entire arterial system with each systole of the heart can be perceived in certain localities by the eye, by the sense of touch, and investigated with various forms of apparatus or instrumental means. The pulse-wave, or at least the elevation of the soft tissues overlying it, can be seen in the radial artery, where it passes across the wrist-joint, in the carotid artery, in the temporal artery, and in the arteries of the retina under certain conditions, with the ophthalmoscope.

The Radial Pulse.—If the ends of the fingers are firmly placed over the radial artery, not only the increase and decrease of pressure, but also many of the peculiarities of the pulse-wave, may be perceived. Without much difficulty it may be perceived that the expansion takes place quickly, the recoil relatively slowly; that the waves succeed one another with a certain frequency, corresponding to the heart-beat; that the pulsations are rhythmic in character, etc.

Inasmuch as the individuality of the pulse-wave varies at different periods of life and under different physiologic and pathologic conditions, various terms more or less expressive, have been suggested for its varying qualities. Thus the pulse is said to be *frequent* or *infrequent* according as it exceeds or falls short of a certain average number—72 per minute; *strong* or *weak* according to the energy with which the vessel expands; *quick* or *slow*, according to the suddenness with which the expansion takes place or strikes the fingers; *hard* or *soft*, *tense* or *easily compressible*, according to the resistance which the vessel offers to its compression by the fingers; *large*, *full* or *small*, according to the volume of blood ejected into the aorta, or, in other words, the degree of fullness of the arterial system.

The three qualities which are of most value to the clinician are rate, strength or force, and volume.

Frequency of the Pulse.—As the pulse or the arterial expansion and recoil is the direct result of the heart's action, its frequency must, under physiologic conditions, coincide with that of the heart. (See page 290.) All conditions which modify the rate of the heart will modify at the same time the rate of the pulse.

For the purpose of accurately studying and analyzing the pulse-wave and its characteristic features, it is necessary to obtain graphic records of the alternate expansion and recoil of the artery under normal and abnormal conditions. This is accomplished by means of—

The Sphygmograph.—The sphygmograph is, therefore, an apparatus designed to take up, reproduce, and record the alternate expansion and recoil of an artery caused by the temporary increase and decrease of pressure following each heart-beat. The tracing or record obtained with it is termed the *pulse-curve* or the *sphygmogram*. Different forms of this apparatus have been devised by Marey, Dudgeon, v. Frey, and many others. The instrument of v. Frey is shown in Fig. 172. This consists, first, of a metal framework *GS* by which the apparatus is fastened to the arm and support given to the lever, recording surface, etc. The essential part is the spring carrying a button *P*, which is placed over the artery, usually the radial, before it crosses the wrist-joint. A vertical rod *F* transmits the movement of the spring to the recording lever; the movements of the latter are recorded on a small cylinder inclined slightly so that the upstroke may be vertical. A small electro-magnet serves to record the time relations of the changes in the blood-pressure. The artery usually selected for obtaining a sphygmogram is the radial. This artery lies quite superficially, is covered only by connective tissue and skin and is supported by the flat surface of the radial bone, conditions most favorable to technical investigation. When the apparatus is properly adjusted a tracing similar to that

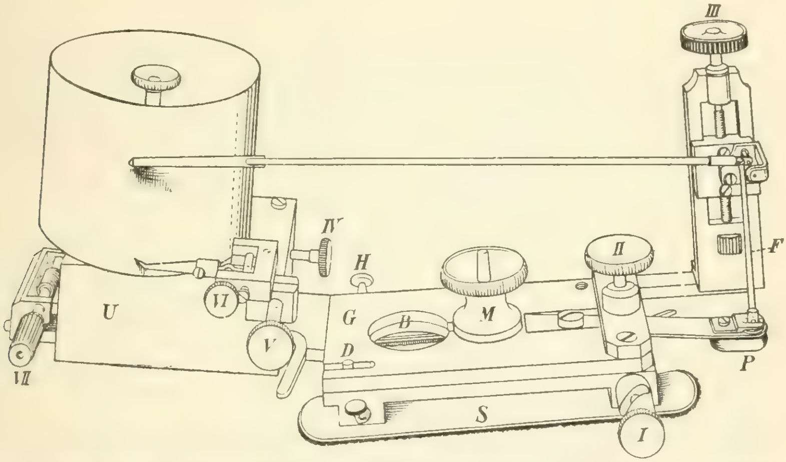

Fig. 172.—Von Frey's Sphygmograph. *GS*. Metal framework. *P*. Button attached to spring. *F*. Vertical rod. *U*. Clock-work which turns the recording cylinder. *VI*. Time marker.

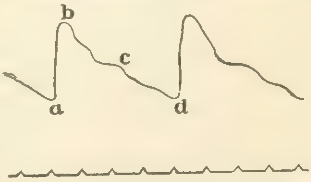

Fig. 173.—The Pulse-curve or Sphygmogram of the Radial Artery.

shown in Fig. 173 is obtained. This, however, is not a tracing of the pulse wave, but rather a record of the changes in pressure, their succession and time relations, which follow each beat of the heart.

The sphygmogram or pulse-curve may be divided into two portions: viz., a line of ascent from a to b, the *anacrotic*, and a line of descent from b to d, the *catacrotic* (Fig. 170). In normal tracings the former is almost vertical and caused by the sudden expansion of the artery immediately following the ventricular contraction; the latter is in general oblique, occupies a longer period of time, due to the slow recoil of the arterial walls, and is marked by several elevations and depressions, both of which indicate that the restoration to equilibrium is neither immediate nor uncomplicated. One of these elevations is quite constant and known as the *dicrotic wave*, c; the depression or notch just preceding it is known as the *dicrotic notch*. Pre- and post-dicrotic waves are not infrequently present. The summit is generally sharp and pointed.

The vertical direction of the line of ascent is taken as an indication that the arterial walls expand readily, that the blood is discharged quickly, and that the ventricular action is not impeded. An oblique direction of the line of ascent is an indication that the reverse conditions obtain. The height varies inversely as the arterial pressure, other things being equal; being high with a low pressure, and low with a high pressure.

The dicrotic elevation shows that a second expansion wave is developed which interrupts temporarily the recoil of the arterial walls. The origin of this second expansion has been the subject of much investigation, and at present it may be said that the question is not fully decided. It is asserted by some investigators that it is central in origin, beginning at the base of the aorta and passing to the periphery; by others, that it is peripheral in origin, beginning near the capillary region and reflected to the heart. The former view is the one more generally accepted. According to it, the expansion is the result of the sudden closure of the aortic valves, and a backward surge of the blood column against them. The sudden arrest of the blood and its accumulations again expands the aorta.

The dicrotic notch is, therefore, taken as the moment at which the ventricular systole ceases and the aortic valves close. From this fact it is evident that immediately after the first expansion the pressure begins to fall, even though the ventricular systole continues, owing to the discharge of blood from the arterial into the capillary and venous systems. The height of the dicrotic wave or the depth of the dicrotic notch is increased by low arterial pressure and highly elastic arteries. Both features are diminished by the reverse conditions. The apex is sometimes rounded and even flat, indicative of a great diminution in arterial elasticity. The sphygmogram not infrequently varies considerably from the normal type in different pathologic conditions of the circulatory apparatus. A consideration of these variations does not fall within the scope of this work.

The Carotid Pulse.—The carotid pulse can be readily recorded by applying over the carotid artery, anterior to the sternocleidomastoid muscle, on a level with the thyroid cartilage, a funnel-shaped tambour in connection with a suitable recording tambour and lever. The sphygmogram thus obtained resembles in all essential respects that obtained from the radial artery. It is often of advantage in the investigation of certain problems of the heart, both physiologic and pathologic, to record the carotid pulse and the cardiac impulse simultaneously.

The Venous Pulse.—By this term is meant a pulsation of the large veins in the neighborhood of the heart but more especially in the jugular veins. It is caused by variations of pressure transmitted backward into the veins during and after the systole of the auricle. Though the venous pulsation is not very marked in physiologic conditions it frequently becomes pronounced in certain pathologic conditions of the heart.

The pressure variations in the jugular vein can be recorded by applying over the vein a properly constructed tambour, a glass funnel or a Mackenzie metal tambour connected with a suitable recording tambour. A graphic record of a normal venous pulse thus obtained, shown in Fig. 174, is rather complicated, consisting of three positive and three negative waves which are related to variations of pressure in the right auricle, the result of the successive contractions of the auricular and ventricular walls and the action of intra-ventricular structures.

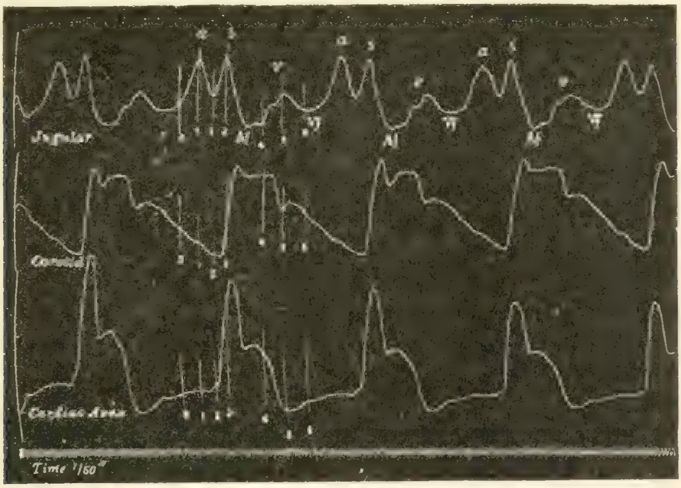

FIG. 174.—SIMULTANEOUS TRACINGS OF THE JUGULAR PULSE, THE CAROTID PULSE, AND THE APEX BEAT.—(*Bachmann.*) At the bottom of the tracing the time is given in the fiftieths of a second. The vertical lines 0, 1, 2, 3, etc., mark synchronous points on the curves. *A*, The auricular wave; *s*, the so-called *c* wave caused by the systole of the ventricle; *v*, the stagnation wave caused by the filling of the auricle. It will be noticed that the *c* wave (marked *s* in the tracing) occurs at the beginning of the ventricular systole as marked on the apex beat, and shortly before the pulse in the carotid artery. The height of the *v* wave is reached just after the occurrence of the dicrotic notch on the carotid wave, and coincides with the opening of the auriculo-ventricular valves; *Af*, the negative wave caused by the effect of the ventricular systole; *Vf*, the negative wave following the opening of the auriculo-ventricular valves.

As the venous pulse is a very evident symptom in some pathologic conditions of the heart, and as its proper interpretation assists in the diagnosis of these conditions, it has become of much significance in modern clinical medicine. For purposes of interpretation it is desirable to obtain simultaneously graphic records not only of the venous pulse, but of the carotid or radial pulse, and of the cardiac impulse as well. In the accompanying Fig. 171 these three records are represented.

The generally accepted interpretation of these waves is as follows:

The *first positive* wave, *a*, is due to an expansion of the vein, the result of a sudden rise of pressure. As it occurs before the ventricular systole, it is pre-systolic in time and caused by the contraction of the auricle, the effect of which is to cause a temporary retardation of the blood-stream flowing toward the auricle and hence a backward wave of pressure.

The *first negative* wave is due to a recoil of the veins following a diminution of the pressure as the blood again moves forward in consequence of the relaxation of the auricular walls.

The *second positive* wave, *c* or *s*, is also caused by a wave of positive pressure in the vein, reflected from the auricle, though it is not of auricular origin. As it begins with the ventricular contraction and develops during the closed period, the protosystolic period, *i.e.*, between the closure of the tricuspid valve and the opening of the semilunar valves (see page 287), it is believed to be due to the bulging of the auriculo-ventricular valve into the auricular cavity, by the still higher intra-ventricular pressure thus diminishing its size and raising its pressure.

The *second negative* wave, *Af*, is due to a marked fall of pressure, a collapse of the walls of the vein and a rapid flow of blood to the auricular cavity. These phenomena begin with the opening of the semilunar valves and are due in part to the relaxation of the auricular walls, but more especially to a descent of the more central portions of the auriculo-ventricular valve or septum, into the ventricular cavity in consequence of the contraction of the papillary muscles. The hollow cone thus formed, enlarges the auricular cavity, withdraws some of its contained blood, and hence lowers the pressure, which leads to the inflow of blood from the veins and hastens the auricular filling.

The *third positive* wave, *v*, is caused by a third wave of pressure reflected from the auricle. It occurs toward the end of the ventricular systole and is probably due to a slight retardation of the blood flow in consequence of the return of the auriculo-ventricular septum to its normal position, the result of a relaxation of the papillary muscles, when the intra-ventricular pressure is still higher than the intra-auricular pressure.

The *third negative* wave, *Vf*, is caused by a third fall of pressure in the vein and appears very shortly after the beginning of the ventricular relaxation, and the closure of the semilunar valves. It develops during the common pause of auricles and ventricles. The fall of the venous pressure follows the passage of the blood from the auricle into the ventricle. It continues during the ventricular filling but disappears on the return of the auricular contraction.

The Volume Pulse.—If an individual artery expands with each systole and recoils with each diastole of the heart, the same is true of all arterie, and as a result the volume of any organ or part of the body must undergo similar changes. To such alternate changes in volume the term *volume pulse* is given. The extent to which an organ will increase in volume will depend to some extent on its elasticity. The reason for the increase in volume is the resistance offered to the flow of blood into and through the capillaries; the decrease in volume to the overcoming of the resistance through the arterial recoil.

The variations in volume may be recorded by enclosing the organ in a rigid glass or metal vessel, which at one point is in communication with a recording apparatus, *e.g.*, a tambour with a lever or a piston recorder with float and writing point. The space between the organ and vessel is filled with normal saline, air, or oil. Such an apparatus is known as a *plethysmograph*. Fig. 175. Many forms of this apparatus have been devised in accordance with the character of the organ—spleen, kidney, etc.—to be investigated, though the principle underlying them is essentially the same. In addition to changes in volume due to the heart's action, most organs undergo additional changes in volume from vaso-motor and respiratory causes.

Indeed the plethysmographic is the most generally employed method of showing the action of vaso-motor nerves in changing the contraction of the arterioles and hence the outflow of blood. Thus when an organ is enclosed in a plethysmograph and the arterial contraction increased by either a direct or reflex stimulation of the vaso-motor center there will be a rise in the pressure, a diminution in the outflow of blood and a decrease in the volume of the organ under observation; and on the contrary, if the arteriole contraction is diminished by a direct or reflex inhibition of the vaso-motor center there will be a fall of pressure, an increased outflow of blood and an increase in the volume of the organ. From this it is learned that the functional activity of an organ which is attended and conditioned by an increased blood-supply is always associated with an increase in volume. On plethysmographic records large undulations are frequently observed which are regarded as of respiratory origin.

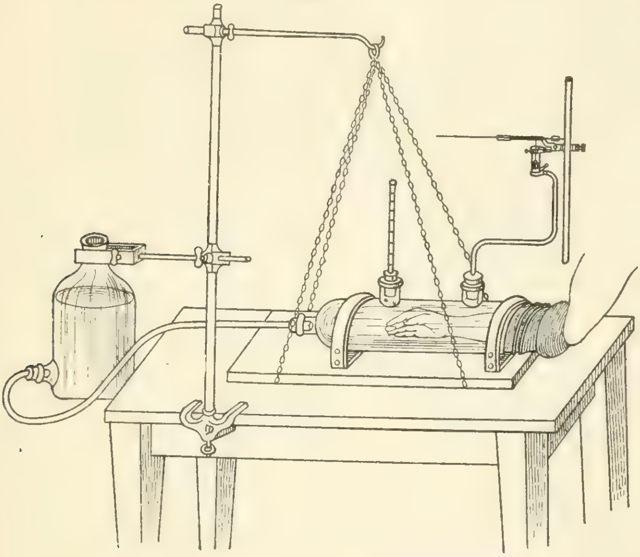

FIG. 175.—A PLETHYSMOGRAPH FOR THE ARM.

THE CAPILLARY CIRCULATION

In certain regions of the body of many animals it is possible, on account of the delicacy and transparency of the tissues, to observe not only the flow of blood through the smaller arteries, capillaries, and veins, but many of the phenomena connected with it, to which reference has already been made. The structures usually selected for the observation of these phenomena are the interdigital membranes (Fig. 176), the tongue, the lung, the bladder, and the mesentery of the frog. Though any one of these structures will afford an admirable view of the blood flow, the mesentery for many reasons is the most satisfactory. For a comparison of the phenomena observed in the cold-blooded animals with those in the warm-blooded animals the omentum of the guinea-pig may be employed. If the frog is the subject of experiment, it should be slightly curarized and the brain destroyed by pithing. The animal is then placed on a small board capable of adjustment to the stage of the microscope. The abdomen is then opened along the side and a loop of intestine withdrawn and placed around a cork ring which surrounds an opening in the side of the frog board. The loop of the intestine should be so placed that it will lie between the observer and the body of the frog. The mesentery thus exposed must be kept moist with normal saline solution.

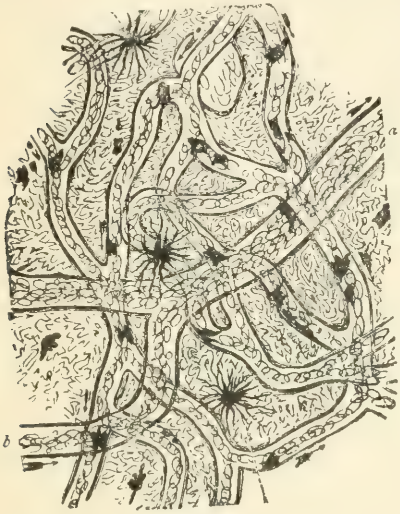

FIG. 176.—THE VESSELS OF THE FROG'S WEB. *a.* Trunk of vein, and (*b*, *b*) its tributaries passing across the capillary network. The dark spots are pigment cells.—(*Yeo's "Physiology."*)

When examined with low powers of the microscope, arteries, veins, and capillaries will be found occupying the field of vision. Their general arrangement, their size and connections, can be readily determined. After a few preliminary adjustments a region will be found in which the blood is flowing in opposite directions. The vessel apparently carrying blood *away* from the observer is an artery; the vessel apparently carrying blood *toward* the observer is a vein; the smallest vessels are capillaries. The blood in the artery is of a brighter color than the blood in the vein; the blood in the capillaries is almost colorless. The arterial blood-stream not infrequently shows remittency, an alternate acceleration and retardation, corresponding to each heart-beat; the capillary and venous streams are uniform and continuous. The relative velocities in the three sets of vessels are indicated by the movement of the red corpuscles. In the arteries they pass before the eye so rapidly that they cannot be distinguished; in the capillaries they pass so slowly that both form and structure may be determined; in the veins, though again moving rapidly, they can often be distinguished.

The relative positions of the red and white corpuscles in the blood-stream are also apparent; the former occupy the central, the latter the peripheral portion, at the same time adhering to the sides of the vessel. Between the axial portion of the stream occupied by the red corpuscles and the wall of the vessel there is a clear still layer of plasma, the result of an adhesion of the plasma to the wall. It is this feature which gives rise to the friction between successive layers of the blood-stream, the resistance of the blood flow, and the development of the blood-pressure. The relative breadth of the still layer and amount of friction are greater in small than in large vessels.

The volume of blood passing into any given capillary area is determined by the degree of contraction of the arterioles. Thus on the application of warm saline solution, which relaxes the arterioles, there is a large increase in the inflow of blood; vessels previously invisible suddenly come into view as the blood with its corpuscles passes into them. On the application of cold water, which contracts the arterioles and diminishes the inflow, many of the smaller vessels entirely disappear from view. The contraction and relaxation of the arterioles will therefore determine the quantity of blood flowing into and through the capillary system.

Migration of the White Corpuscles.—A phenomenon frequently observed in the capillary vessels of the mesentery or of the bladder of the frog is the passage of the white corpuscles through the walls into the surrounding lymph-spaces. To this process the term *migration* or *diapedesis* is given. After the tissues have been exposed to the air for some time or subjected to an irritant, the vessels dilate and become distended with blood. In a short time the blood-stream slows, and finally comes to rest. The condition of stasis is then established. During the development of this condition the white corpuscles accumulate in large numbers along the inner surface of the vessels and soon begin to pass through the vessel-walls. This they do by protruding a portion of their substance and inserting it into and through the vessel-wall. This once accomplished, the remainder of the cell in due time follows until it has entirely passed out into the tissue-space. The opening in the vessel-wall now closes. The successive steps in this process are shown in Fig. 177. As this migration occurs mainly after the circulation has ceased or when the tissues present the phenomena of approaching inflammation, it is difficult to state in how far it is strictly a physiologic process.

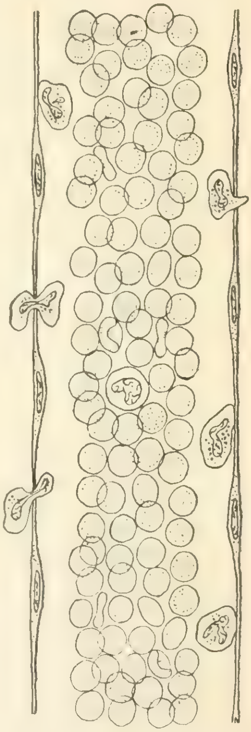

Fig. 177.—Diagram to show Various Stages in the diapedesis or Migration of White Corpuscles.

The Venous Circulation.—The blood, having passed through the capillary vessels, is gathered up by the veins and conveyed to the right side of the heart. As the veins converge and unite to form larger and larger trunks the sectional area gradually diminishes, and hence the velocity of the blood-flow increases, though it never attains the velocity, even in the venæ cavæ, that it had in the aorta, for the reason that the sectional area of the venæ cavæ is considerably larger than that of the aorta. The pressure also is very low in the larger veins because the friction still to be overcome is relatively very slight.

The capacity of the venous system is considerably greater than that of the arterial system, as there are usually two and even three veins accompanying each artery. This, taken in connection with its greater distensibility, makes of the venous system a reservoir in which blood can be stored. On this reservoir the arterial system can call for that amount of blood necessary for the maintenance of its normal volume and pressure, and into it any excess can be discharged. The relative amounts of blood contained in the two systems are regulated by the degree of contraction of the arteriole muscles and this in turn by the vaso-motor nerves. The movement of the blood through the veins is accomplished by the coöperation of several forces, reference to which will be made in a following paragraph.

The Pulmonic Vascular Apparatus.—The pulmonic vascular apparatus consists of a closed system of vessels extending from the right ventricle to the left auricle, and includes the pulmonic artery, capillaries, and pulmonic veins. In its anatomic structure and physiologic properties it closely resembles, with, the systemic apparatus.

The stream-bed widens from the beginning of the pulmonic artery to the middle of the capillary system; it again narrows from this point to the terminations of the pulmonic veins.

The movement of the blood from the beginning to the end of the system is due to a difference of pressure between these two points, the result of the friction between the blood and the vascular walls. The pressure in the pulmonic artery of the dog has been shown by Beutner to be about one-third that in the aorta; by Bradford and Dean to be one-fifth. Wiggers has recently shown that in normally breathing dogs with arterial pressures ranging from 110 to 112 mm. of mercury, the maximal or systolic pressure in the pulmonic artery averaged 36 mm., and the minimal or diastolic averaged 5 mm. The reason for the low pressure may be found in the large size and rich development of the pulmonic capillaries and the imperfect development of an arteriole muscle at the periphery of the pulmonic artery, the result of which is a diminution in the friction. Inasmuch as the friction is relatively low, the work of the right heart is less than that of the left heart and hence its walls are not so well developed. The pulmonic pressure being low the intraventricular pressure of the right heart is relatively low as compared with that of the left heart. The velocity of the blood-stream in each of the three divisions of the system cannot well be determined. The time occupied by a particle of blood in passing from the right to the left ventricle has been estimated at one-fourth the time required to pass from the left to the right ventricle. Assuming the latter to be thirty seconds, the former would be seven and one-half seconds.

The presence of vaso-motor nerves in the walls of the arterioles of the pulmonic artery has not been definitely determined. Adrenalin which constricts blood vessels supplied with vaso-motor nerves is stated by some investigators to have this effect, but by others to be without it. If vaso-motor nerves are present their action is relatively slight.

The capillary vessels are spread out in a very elaborate manner just beneath the inner surface of the pulmonic air-cells, and form, by their close relation to it, a mechanism for the excretion of carbon dioxid and the absorption of oxygen. The extent of the capillary surface is very great. It has been estimated at 200 square meters. The amount of blood flowing through this system hourly and exposed to the respiratory surface is about 430 liters. The reason for the existence of the pulmonary circulation is the renewal of the oxygen in the blood and the elimination of the carbon dioxid; for the accomplishment of both objects ample provision is here made. The flow of blood through the cardio-pulmonary vessels is subject to variation during both inspiration and expiration in consequence of their relation to the respiratory apparatus. The mechanism by which these variations are produced will be considered in the chapter devoted to Respiration.

FORCES CONCERNED IN THE CIRCULATION OF THE BLOOD

1. **The Contraction of the Heart.**—The primary forces which keep the blood flowing from the beginning of the aorta to the right side of the heart and from the beginning of the pulmonary artery to the left side are the contractions of the left and right ventricles respectively. This is evident from the fact that each ventricle at each contraction not only overcomes the pressure in the aorta and pulmonary artery, the sum of all resistances, but imparts a given velocity to the blood. Since the pressure continuously falls from the beginning to the end of each system, it follows that the blood must flow from the point of high to the point of low pressure. During the interval of the heart's activity, the walls of the arteries, to which the heart's energy was largely transferred, now take up and continue the work of the heart, and by recoiling drive the blood forward and into the venous system. Though the heart's energy is probably sufficient to drive the blood into the opposite side of the heart, it is supplemented by other forces—*e.g.*:
2. **Muscle Contraction.**—As a result of the relation which the veins bear to the muscles in all parts of the body it is clear that with the contraction and relaxation of the muscles there will be exerted an intermittent pressure on the veins. With each contraction, the blood on the proximal side will at once be driven forward with increased velocity, while that on the distal side will be retarded, will accumulate and distend the veins, owing to the closure of the valves; with the relaxation of the muscle the elastic and contractile tissues in the walls of the veins will come into play and force the blood forward.
3. **Thoracic Aspiration.**—The inspiratory movement aids the flow of blood through the venæ cavæ and their tributaries. With each inspiration the pressure within the thorax but outside the lungs undergoes a diminution more or less pronounced in accordance with the extent of the movement. As a result, the blood in the large veins outside of the thorax, being subjected to a pressure greater than that in the thorax, flows more rapidly toward the heart. With each expiration the reverse obtains.
4. **Action of the Valves.**—It is quite probable that gravity opposes to some extent the flow of blood through the veins below the level of the heart. This opposition to the upward flow is largely prevented by the valves, for each retardation is immediately checked by their closure and support given to the column of blood. The influence of gravity is shown when the relation of the arm to the heart is changed. Thus,

if the arm be allowed to hang passively by the side of the body, the veins, as seen on the back of the hand, will become distended with blood. If now the arm be raised, the blood will flow rapidly toward the heart, as shown by the rapid emptying of the veins.

Work Done by the Heart.—The work which the left ventricle performs at each contraction when it discharges its contained volume of blood into the aorta is:

1. To overcome the total resistance of the systemic vascular apparatus.
2. To impart velocity to the blood.

The resistance may be expressed in terms of aortic pressure. The pressure in the aorta has not been absolutely determined, though for many reasons it may be assumed to be about 150 mm. Hg., or its equivalent, a column of blood 1.93 meters in height. If the volume of blood which the heart discharges is assumed to be 83 grams, the work done may be calculated by multiplying the weight by the height to which it is raised: viz., $0.083 \times 1.93 = 0.16019$ kilogrammeter.

The velocity of the blood in the aorta has been approximately estimated at 0.5 meter per second. The work done in imparting this velocity to 83 grams is estimated by squaring the velocity and dividing by the accelerating force of gravity $(\frac{0.5^2}{2 \times 9.81})$ and multiplying the quotient by 0.083. The value of the fraction given above represents the distance a body would have to fall to acquire this velocity: viz., 0.0127 meter. The work done is therefore 0.083×0.0127, or 0.01054 kilogrammeter.

The entire work of the left ventricle is the sum of these two amounts, or 0.17073 kilogrammeter. Assuming that the heart beats 72 times per minute, the work done daily would be $0.17073 \times 72 \times 60 \times 24$, or 17701.3 kilogrammeters. The right ventricle approximately performs one-third of this amount of work in overcoming the resistance offered by the pulmonary system and in imparting velocity to its contained volume of blood. The work of the entire heart would therefore be for the twenty-four hours about 23,600 kilogrammeters.

THE NERVE MECHANISM OF THE VASCULAR APPARATUS

By this expression is meant a combination of nerves and nerve-centers by which the rate and force of the heart contractions and the contraction of the arteriole muscles are maintained. It includes the cardiac nerves (the cardio-accelerator and the cardio-inhibitor) and the vascular or vasomotor nerves (the vaso-augmentor or constrictor and the vaso-inhibitor or dilatator nerves). The function of this mechanism is to maintain the high blood-pressure characteristic of the arterial system, and to regulate from moment to moment, the quantity of blood flowing into and out of organs in accordance with their functional activities. The cardiac nerves have been considered on pages 312–313.

Arterial Tonus.—The arteries, especially those in the peripheral region of the arterial system, possess a well-defined layer of non-striated muscle-fibers arranged in a circular direction or at right angles to the long axis of the vessel. In the physiologic condition these arterioles are distended beyond the natural condition by the side pressure of the blood flowing through them, at the same time the muscle-fibers are in a state of tonic contraction, thus giving to the arteries a certain average caliber which permits a definite volume of blood to flow through them in a given unit of time. To this condition of the arterial wall the term tonus is applied.

The cause of this tonic contraction is not definitely known. It has been attributed to the action of local nerve-ganglia, to the pressure of blood from within, to the influence of organic substances in the blood, the products of gland activity: *e.g.*, adrenalin or epinephrin.

This tonic contraction of the vascular muscle is subject to increase or decrease, to augmentation or inhibition, in accordance with the action of various agents. An augmentation of the contraction will result in a decrease of the caliber and a reduction in the outflow of blood. An inhibition of the contraction or relaxation will result in an increase both of the caliber and outflow of blood. The small arteries thus determine the volume of blood passing to any given area or organ in accordance with its functional activities.

The Vaso-motor Nerves.—The activities of the vascular muscle are regulated by the central nerve system through the intermediation of nerve-fibers, termed *vaso-motor* nerves. Of these there are two kinds, one which increases or augments the contraction, the *vaso-constrictors* or *vaso-augmentors;* and another which decreases or inhibits the contraction, the *vaso-dilatators* or *vaso-inhibitors.*

The Vaso-constrictor Nerves.—The vaso-constrictor nerves take their origin from nerve-cells located in the anterior horns and lateral gray matter of the spinal cord. They emerge from the cord in company with the fibers that compose the ventral roots of the spinal nerves from the second thoracic to the second or third lumbar nerves inclusive. A short distance from the cord they leave the ventral roots as the white rami communicantes and enter for the most part the vertebral or lateral sympathetic ganglia. From the results of many observations and experiments it is probable that the great majority of the vaso-constrictor nerves terminate in these ganglia; that is to say, it is here that the pre-ganglionic fibers arborize around the contained nerve-cells. From the nerve-cells new fibers arise, the post-ganglionic, which pass to the blood-vessels of (1) the body walls; (2) the fore limbs; (3) the head, neck and face; (4) the hind limbs; and (5) the abdominal viscera.

1. The vaso-constrictors for the blood-vessels of the walls of the trunk of the body emerge from the spinal cord in the ventral roots of the spinal nerves from the second thoracic to the third lumbar nerves inclusive. After a short course they leave the ventral roots and pass by way of the white rami into the corresponding thoracic and lumbar ganglia around the nerve-cells of which they arborize. From these ganglia new nerve-fibers arise which pass back by way of the gray rami, into the thoracic and lumbar nerves and in association with them pass directly to the blood-vessels of the skin. (Fig. 178 *A*.)
2. The vaso-constrictors for the blood-vessels of the fore limbs emerge from the spinal cord in the ventral roots of the fourth to the tenth thoracic nerves inclusive. After a short course they leave the ventral roots, pass into the white rami, thence into the sympathetic chain, after which they take an upward direction and terminate around the cells of the ganglion stellatum. From this ganglion the new nerve-fibers enter by way of the gray rami, the trunks of the cervical nerves which unite to form the

brachial plexus and by this route pass to the blood-vessels of the skin and possibly of the muscles of the fore limb.

3. The vaso-constrictors for the blood-vessels of the head, face and neck emerge from the spinal cord in the ventral roots of the first four thoracic nerves. After a short course they leave the ventral roots by way of the white rami and pass into the sympathetic chain after which they pass upward through the ganglia and cord to the superior cervical ganglion, around the cells of which these fibers arborize. From this ganglion new fibers arise which follow the carotid artery and its branches to their superficial terminations at least (Fig. 178 *B*).

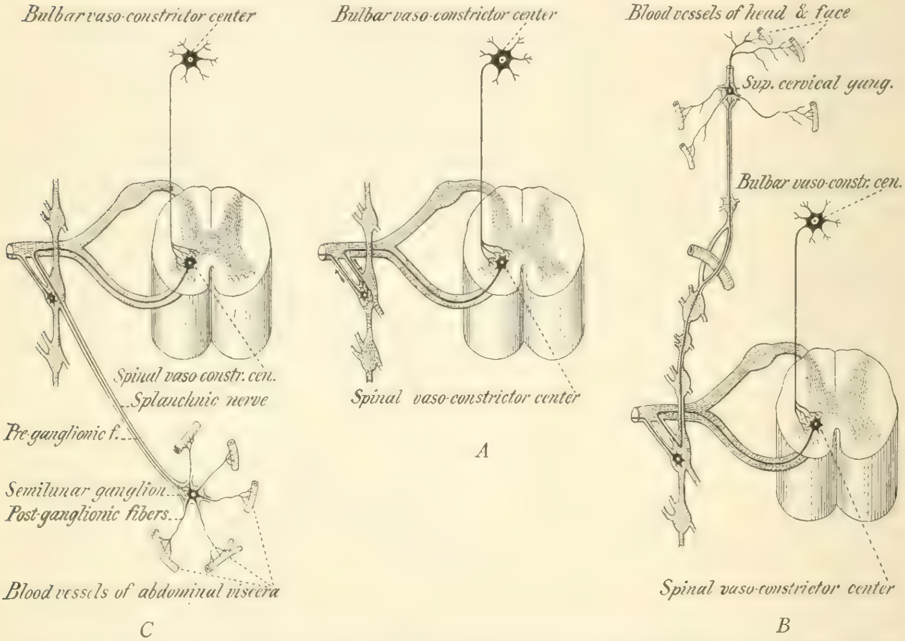
Bulbar vaso-constrictor center
Bulbar vaso-constrictor center
Blood vessels of head & face
Sup. cervical gang.
Bulbar vaso-constr. cen.
Spinal vaso-constr. cen.
Splanchnic nerve
Pre-ganglionic f.
Semilunar ganglion
Post-ganglionic fibers
Blood vessels of abdominal viscera
Spinal vaso-constrictor center
A
Spinal vaso-constrictor center
C
B

FIG. 178.—Diagrams showing the course of the pre- and post-ganglionic vaso-motor fibers for the blood-vessels; of *A*, the walls of the trunk of the body; of *B*, the head and face; and of *C*, the abdominal viscera.

4. The vaso-constrictors for the blood-vessels of the hind limbs emerge from the spinal cord in the ventral roots of the tenth thoracic to the second or third lumbar nerves inclusive. They then pass by way of the white rami into the corresponding ganglia around the nerve-cells of which some of the fibers arborize. Others, however, descend the sympathetic chain to terminate in successive ganglia as far as the third sacral ganglion. From all these ganglia new nerve-fibers arise which pass backward into the corresponding nerves which enter into the formation of the lumbar and sacral plexuses and by this route reach the blood-vessels of the skin of the lower portions of the trunk and hind limbs.

5. The vaso-constrictors for the blood-vessels of the viscera of the abdominal cavity emerge from the spinal cord in the ventral roots from the fifth thoracic downward. After leaving these roots by way of the white rami they pass into and across the ganglia composing the thoracic por-

tion of the sympathetic chain and by their union subsequently assist in the formation of the splanchnic nerves the terminal fibers of which arborize around the cells of the collateral ganglia, viz.: the semilunar, superior mesenteric renal, etc. From these various ganglia an elaborate network of non-medullated fibers passes to the blood-vessels of the stomach, intestines, and other viscera. The great splanchnic nerve is one of the most important vaso-constrictor trunks of the body, on account of the large vascular area it controls (Fig. 178 *C*).

The existence, course, distribution, and functions of the vaso-constrictor nerves have been determined by a variety of methods, physiologic and anatomic. Stimulation of the nerve trunks under appropriate conditions gives rise to a contraction, division to a dilatation of the blood-vessels. The physiologic continuity of the pre-ganglionic fibers with the nerve-cells of the sympathetic ganglia has been shown by the intra-vascular injection or the local application of nicotin. This agent, as shown by Langley, has a selective action on the arborizations of the pre-ganglionic fibers, and when given in sufficient doses suspends their conductivity; hence stimulation of pre-ganglionic fibers is without effect, though stimulation of the post-ganglionic fibers is followed by the usual contraction.

The following facts will serve as illustrations of the functions of vaso-constrictor nerves. Division of the great splanchnic is followed by a marked dilatation of the blood-vessels of the intestinal tract and a decided fall in blood-pressure; stimulation of the peripheral end by their contraction and a marked rise in blood-pressure. Division of the cervical cord of the sympathetic is followed by dilatation of the blood-vessels of the side of the head; stimulation of the peripheral end by their contraction.

The Vaso-dilatator Nerves.—The vaso-dilatator nerves have been found in some of the cranial nerves and in association with vaso-constrictor fibers in most of the nerve trunks of the body. Thus they have been found in the nerve of Wrisberg, the glosso-pharyngeal, in the nerve trunks of the upper and lower limbs, of the body walls, of the abdominal viscera (the splanchnic nerve) and of the pelvic viscera.

The vaso-dilatator nerve-fibers that are found in some of the cranial nerves have their origin in nerve-cells in the gray matter of the medulla oblongata. From these cells they pass out in the trunk of the *pars intermedia* or nerve of Wrisberg and in the trunk of the glosso-pharyngeal nerve. Those fibers which are contained in the nerve of Wrisberg, enter, after a short course, the trunk of the facial nerve and through its branches the great petrosal and the chorda tympani, are ultimately distributed as pre-ganglionic fibers to the spheno-palatine and submaxillary ganglia respectively. From the spheno-palatine ganglion cells post-ganglionic fibers are distributed to the blood-vessels of the mucous membrane of the nasal chambers posteriorly, and to adjacent regions. From the submaxillary ganglion post-ganglionic fibers pass to the blood-vessels of the submaxillary and sublingual glands.

The vaso-dilatator fibers that are contained in the glosso-pharyngeal nerve pass through the tympanic plexus by way of Jacobson's nerve to the otic ganglion, around the cells of which their end branches arborize; from the cells of this ganglion post-ganglionic fibers pass to the walls of the blood-vessels of the parotid gland and of the cheek and gums.

The vaso-dilatator nerve-fibers that are found in some of the sacral nerves have their origin in nerve-cells in the gray matter of the lumbar or sacral region of the spinal cord. From these cells they pass into the ventral roots of the second and third sacral nerves to be ultimately distributed by way of the pelvic nerve to sympathetic ganglia in the pelvic region around the cells of which their terminal branches arborize. From these ganglia post-ganglionic fibers emerge which pass to the blood-vessels of the organs of generation and adjacent structures.

Antidromic Vaso-dilatator Nerve-fibers.—Vaso-dilatator nerve-fibers are associated with the vaso-constrictor fibers and are present in the trunks of the spinal nerves and are distributed to the blood-vessels of the skin of the limbs and trunk. Though it has been generally believed that these vaso-dilatator fibers have their origin in nerve-cells in the ventral horns of the gray matter, that they pass outward through the ventral roots of the thoracic and lumbar nerves, that they belong to the efferent system of nerves, yet these facts have never been positively determined. While this may be the correct interpretation doubt has been thrown upon it by the investigations of Bayliss. From the results of a long series of experiments this investigator concludes that vaso-dilatator nerves for the regions of the body just mentioned, do not leave the spinal cord in the ventral roots; that the vaso-dilatation observed on stimulation of the mixed spinal nerve is due to the presence of nerve-fibers that do not differ from the ordinary afferent or sensor, posterior or dorsal root fibers; that these nerve-fibers, moreover, have their origin in the nerve-cells of the ganglia of the dorsal roots. From the fact that they transmit nerve impulses to blood-vessels in a direction contrary to that of other afferent nerve-fibers, the term *antidromic* has been given to them. The centers from which they arise are capable apparently of being aroused to activity by impulses transmitted to them from other regions of the body.

These statements are based on the following facts: Stimulation of the peripheral ends of the divided dorsal roots of the upper thoracic and lumbo-sacral nerves gives rise to vascular dilatation in the upper and lower limbs; separation from the cord is not followed by their degeneration, hence they are not efferent nerves; extirpation of the ganglia of the dorsal roots is, however, followed by their degeneration, hence their trophic centers are in these ganglia. Whether the blood-vessels of the abdominal viscera which apparently receive vaso-dilatator nerve impulses are supplied by nerves having the foregoing origin and action, is a subject for further investigation.

The course, distribution, and functions of the vaso-dilatator nerves have been determined by the same methods as those employed in the investigation of the vaso-constrictor nerves. Thus division and stimulation of the peripheral branches of the nerve of Wrisberg, *e.g.*, the great petrosal and the chorda tympani, is followed by an active dilatation of the blood-vessels of the nasal chambers and palate, and of the blood-vessels surrounding the submaxillary and sublingual gland. The inflow of blood is so great that the submaxillary gland becomes bright red in color. Its tissues being unable to consume all the oxygen, the blood emerges in the veins almost arterial in color. Stimulation of Jacobson's nerve has the same effect on the blood-vessels of the parotid gland. Stimulation of the branches of the sacral nerves which collectively constitute the *nervus erigens* is followed by a dilatation of the blood-vessels of the sexual organs.

Slow stimulation of the peripheral ends of various spinal nerves is followed by dilatation of the blood-vessels in the areas to which they are distributed.

From these and many other facts of a similar character it is probable that the blood-vessels of some of the organs at least are under the control of two antagonistic classes of nerve-fibers, one augmenting the degree of their contraction (the vaso-constrictors), the other diminishing it through inhibition (the vaso-inhibitors). Through the coöperative antagonism of these two classes of nerves the caliber of the blood-vessels and thereby the volume of the blood is accurately adapted to the needs of each organ both during rest and during activity. It is also to the alternate activity of these nerves that the variations occurring from time to time in the volume of organs are to be attributed.

A general *vaso-dilatator* center has never been located and there are many reasons for thinking that such a center has no anatomic existence. There are, however, special or local vaso-dilatator centers in the medulla oblongata and in various regions of the spinal cord especially in the sacral region.

Physiologic Properties of Vaso-motor Nerves.—The vaso-constrictor and the vaso-dilatator nerve-fibers differ somewhat in their physiologic properties, as shown by the results of experiment. Thus, when a mixed nerve, *i.e.*, one containing both classes of fibers—*e.g.*, the sciatic—is stimulated with frequently repeated induced currents, the constrictor effect is the more pronounced, the dilatator effect being wanting or prevented; when stimulated with slowly repeated induced currents, the dilatator effect is the more pronounced. These different effects are strikingly shown in Fig. 179, *A* and *B*.

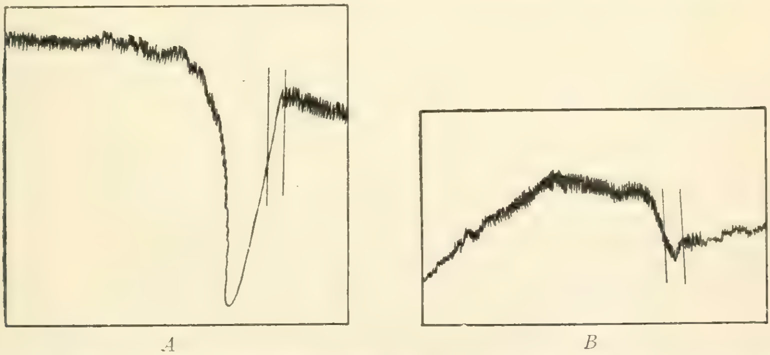

FIG. 179.—PLETHYSMOGRAMS OF THE HIND-LEG OF THE CAT FOLLOWING STIMULATION OF THE SCIATIC NERVE. In *A* the rate of stimulation was sixteen per second, in *B* one per second for fifteen seconds. To be read from right to left. (Boroditch and Warren.)

In the experiment of which these tracings are the result the leg of a cat was enclosed in a plethysmograph and the variations in volume due to dilatation or contraction of the vessels, following stimulation of the sciatic nerve, were recorded by means of tambour and lever on a slowly revolving cylinder. In *A* the fall of the curve indicates a diminution of volume, from contraction of blood-vessels following a rate of stimulation of the sciatic nerve of 16 per second for fifteen seconds. In *B* the rise of the curve indicates an increase in volume from dilatation of the vessels following a rate of stimulation of 1 per second for fifteen seconds. With different rates of stimulation somewhat different results are obtained.

After division of a mixed nerve the vaso-constrictors degenerate and lose their influence over the blood-vessel in from four to five days, the vaso-dilatators in from seven to ten days, as shown by the response to electrical stimulation.

When a nerve is cooled, the vaso-constrictors lose their irritability before the vaso-dilatators.

Vaso-constrictor Centers.—The nerve-cells throughout the spinal cord from which the vaso-constrictor nerves take their origin may be regarded as nerve-centers which through their related nerve-fibers cause a varying degree of contraction of the arteriole muscle. In how far these centers are independent in their activity it is difficult to state. From the results of experiments that have been made with a view of isolating these centers, such as division of the cord at different levels, it is fairly well proven that they respond to nerve impulses transmitted to them from different regions of the body, as shown by the contraction of blood-vessels. This is especially true of lower animals such as the frog and it may possibly be true of mammals. Though it is probable that the spinal vaso-constrictor cells possess a certain degree of tonicity, nevertheless they are subordinate in their activity to, and dominated by, a group of nerve-cells in the upper part of the floor of the fourth ventricle, and termed for this reason the medullary bulbar vaso-constrictor center.

Though the blood-pressure falls to a very low level after the separation of the medulla from the spinal cord, the animal, if properly cared for, may survive the operation and live for a considerable time. Under these circumstances the arteries gradually recover their former degree of contraction. This is accepted as evidence that the nerve-cells in the spinal cord have acquired an independent activity, or developed an activity that had hitherto been dormant. After this, these nerve-centers can be excited to activity by nerve impulses transmitted from the periphery.

The Medullary or Bulbar Vaso-constrictor Center.—The existence of such a dominating center has been determined experimentally: thus if a definite region of the medulla oblongata is punctured or in anyway destroyed there is an immediate dilatation of the blood-vessels throughout the body and a fall of blood-pressure below one-half or one-third of the normal value. This region has a width of one and a half millimeters and extends longitudinally for a distance of four or five millimeters, terminating at a point four millimeters above the tip of the calamus scriptorius. Because of the effects that follow the destruction of this area the anatomic existence of a general vaso-constrictor center has been assumed.

A transection of the medulla above the upper limit of this area is without effect on the blood-pressure. A similar section below it, however, is at once followed by vascular dilatation, a loss of vascular tone, and a general fall of blood-pressure. Subsequent stimulation of the peripheral end of the divided medulla, the animal being curarized and artificial respiration maintained, will give rise to a marked contraction of the blood-vessels and a rise of blood-pressure up to and far beyond the normal value.

If the experimental lesion is limited to the area mentioned in the foregoing paragraph, the vascular dilatation also passes away after a time, the blood-vessels regain their normal tone, and the pressure again rises. These and the foregoing facts indicate that there is in the gray matter beneath the floor of the fourth ventricle a restricted area composed of nerve-cells, which maintains through efferent nerve-fibers the tonus of the blood-vessels by virtue of its dominating influence over the vaso-motor centers in the cord, and which is therefore to be regarded as the *general vaso-motor* (*constrictor*) *center*. The vaso-motor centers throughout the cord are to be regarded as subsidiary centers. The nerve-fibers which transmit the regulative nerve impulses from the general to the subsidiary centers are to be found in the lateral columns of the spinal cord.

The Tonic Activity of the General Vaso-constrictor Center.—Since the blood-vessels maintain a more or less constant tone in the physiologic condition, it is assumed that the vaso-motor center is in a state of continuous or tonic activity or tonus, and as a result continuously discharging nerve impulses through vaso-constrictor nerves to the blood-vessels. The causes of this activity or tonicity have been difficult to formulate. It may be accepted, however, from the results of experimentation that the activity of the center is maintained (1) by the chemic character of the blood and lymph by which it is surrounded and (2) by a continuous inflow of nerve impulses transmitted from all regions of the body, or to both. The following facts will show that both factors are probably involved.

The group of nerve cells which collectively constitute the vaso-motor center has been shown by the experiments of Porter to consist of two groups or centers, viz., a *vaso-tonic center* which maintains the vascular tonus, and a *vaso-reflex* center which permit of various vaso-motor reflexes. After the administration of curara the depressor and sciatic reflex changes in blood-pressure are more than double, while the arterial tonus remains substantially unchanged. Alcohol on the contrary diminishes or removes reflex activity, but leaves the tonus unchanged.

Central Stimulation of the Vaso-tonic Center.—The general vaso-motor (constrictor) center at least is markedly influenced by the quantity and quality of blood and lymph circulating around and through it. If the blood-supply to the medulla and associated structures be diminished by compression of the carotid arteries, the activity of the center is at once increased, as shown by a rise of pressure, the result of increased vascular contraction. Restoration of the blood-suply is followed by a return of the center to its normal degree of activity. An increase of the percentage of carbon dioxid in the blood or a decrease in the percentage of oxygen increases the activity of the center. In asphyxia, a condition in which there is a deficiency in the elimination of carbon dioxid and an insufficiency in the absorption of oxygen the center becomes extremely excitable as shown by the rapid rise of the arterial pressure. By reason of these and other facts it is assumed that the presence and the normal pressure of CO_2 in and around the vaso-motor center is the efficient stimulus to its activtiy. In compression of the carotid arteries as well as in asphyxia, the CO_2 is not removed from the center sufficiently rapidly and hence its pressure increases and unduly excites the center as shown by the rapid rise of the blood-pressure. The subsidiary centers in the spinal cord are influenced by corresponding conditions.

Reflex Stimulation of the Vaso-reflex Center.—The results of experimentation render it certain that the vaso-reflex center may be augmented or inhibited in its activity, and hence followed by increased or decreased vascular contraction, by nerve impulses transmitted to it from the brain, or from the periphery through afferent nerves. The effects may be local and confined to the area in which the stimulus is acting or they may be general. The following experiments may be cited in illustration:

Psychic states of an affective or emotional character influence the activity of this center, doubtless as a result of the arrival of nerve impulses from the cortex of the cerebrum. Thus it is well known that fear causes a contraction of the blood-vessels of the head and face and that shame causes a dilatation of the same vessels. With the cessation or the disappearance of the emotional state, the blood-vessels return to their former degree of contraction.

Stimulation of the central end of a divided posterior root of a spinal nerve gives rise to increased vascular contraction, as shown by the rise of blood-pressure. Stimulation of the central end of the divided sciatic will give rise to opposite results, according to the strength of the stimulus, weak stimuli producing dilatation, strong stimuli producing contraction of the vessels. Stimulation of the central end of the divided vagus gives rise to dilatation of the vessels of the lips, cheeks, and nasal and palatal mucous membranes. Stimulation of the tongue is followed by dilatation of the vessels of the submaxillary gland. Stimulation of certain branches of the vagus nerve is followed by a passive dilatation of blood-vessels and a marked fall of pressure.

The preceding statements as to the effects on the degree of vascular contraction, and hence on the blood-pressure which follow stimulation of different afferent nerves, has lead to the assumption that there are in most afferent nerves two classes of nerve-fibers, though perhaps in varying proportions, one of which when in activity augments, the other of which when in activity inhibits the activity of the vaso-constrictor center. The former class is generally termed *pressor* or *excitator*, the latter *depressor* or *inhibitor fibers*.

Theories of the Mode of Action of the Vaso-motor Centers.—A satisfactory explanation of the manner in which peripheral stimuli influence the activity of the vaso-motor centers and thus bring about the opposite results mentioned in the foregoing paragraphs is difficult to present. Several interpretations have been offered, viz.:

1. The peripheral stimuli according to their qualities act on either the terminals of the pressor or the depressor fibers; according as they do, will the vaso-constrictor center be augmented or inhibited in its activity and followed by either an increase or decrease in the degree of the previous vascular contraction.
2. The peripheral stimuli act simultaneously on the terminals of both pressor and depressor fibers, and hence the vaso-constrictor center is acted on simultaneously by two antagonistic influences. The resulting effect on the blood-vessels, viz., increased or decreased contraction will be the resultant of the action of these two influences on the vaso-constrictor center. If the stimuli act preponderantly on the pressor fibers, the vaso-constrictor center will still be excited; if they act proponderantly on the depressor fibers the center will be inhibited, though in either case not to the same degree as in the first instance.
3. The peripheral stimuli may act on the terminals of the pressor fibers alone. The nerve impulses thus developed are transmitted to both centers but

their effect will be to *excite* the activity of the vaso-constrictor centers and to *inhibit* the activity of the vaso-inhibitor centers; or the peripheral stimuli may act on the terminals of the depressor fibers alone. The nerve impulses thus developed are likewise transmitted to both centers but their effect will be to *inhibit* the activity of the vaso-constrictor centers and to *excite* the activity of the vaso-inhibitor centers. In this view it is assumed that both centers are continuously active and in a state of tonus, and that for the necessary vascular reaction one center must be stimulated, and the other be inhibited. As to which center will be stimulated or inhibited, will probably depend on the character of the stimulus. Hence, the general vascular tonus as well as its variations from time to time, in whole or in part, is the resultant of the simultaneous activity and variations in activity of these two mutually antagonistic but coöperative centers.

Local Special Vaso-dilatator Centers.—The vaso-dilatator centers in the medulla oblongata and in the sacral region of the spinal cord, which give origin to nerve-fibers that regulate the blood-supply to the salivary glands on the one hand and to the generative organs on the other hand as previously stated (page 379) are ordinarily in a condition of relative inactivity and hence the blood-vessels assume a caliber just sufficient to supply the materials necessary to maintain the nutritive activities of the organs concerned. If, however, these centers are aroused to activity, either by nerve impulses descending from the cerebrum in consequence of psychic states of an affective or emotional character, or by nerve impulses transmitted to them through afferent nerves, the blood-vessels of the salivary glands and of the organs of generation, at once actively dilate and the amount of blood they transmit so great that on emerging from the capillaries it still retains its arterial hue. The same phenomena arise if the efferent pre-ganglionic fibers, *e.g.*, the chorda tympani and the nerve of Jacobson, and the nervus erigens or pelvic nerve are stimulated with in-

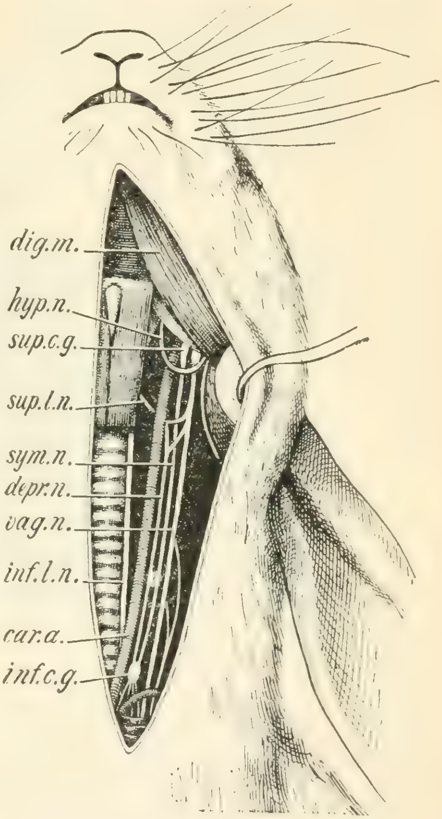

FIG. 180.—DIAGRAM SHOWING THE ORIGIN AND RELATION OF THE DEPRESSOR NERVE IN THE RABBIT. Depr. n., depressor nerve; vag. n., vagus nerve; sup. l. n., superior laryngeal nerve; inf. c. g., inferior cervical ganglion; sym. n., sympathetic nerve; car. a., carotid artery; dig. m., digastric muscle; hyp. n., hypoglossal nerve; sup. c. g., superior cervical ganglion; inf. l. n., inferior laryngeal nerve.

duced electric currents. The organs of generation in consequence of the increased blood flow exhibit changes in volume and rigidity similar to those exhibited previous to the act of coition.

In the particular instances in which stimulation of the peripheral terminations of afferent nerves, associated with the nervus erigens and chorda tympani, is followed by active dilatation of the blood-vessels, it has been assumed that there are afferent nerve-fibers which directly stimulate or augment the activity of the special vaso-dilatator centers and for this reason should be termed "reflex vaso-dilatator nerves" (Hunt).

The Depressor Nerve.—A striking illustration of the depressor or inhibitor action of afferent nerves upon the vaso-constrictor (reflex) center is furnished by the result of stimulation of a branch of the vagus, the so-called "depressor nerve." In the rabbit, Fig. 180, there is a small nerve formed by the union of a branch from the trunk of the vagus with a branch from the superior laryngeal. The peripheral distribution of this nerve is over the wall of the ventricle and perhaps to some extent to the structures of the aorta near its origin. A similar anatomic arrangement is met with in the horse, pig, and hedge-hog. In some other animals, as the dog, it is bound up in the vago-sympathetic. In man it is also present, though shortly after its origin it enters the trunk of the vagus. Division of this nerve is without effect on either the heart or the vessels. Stimulation of the peripheral end has neither an accelerator nor an inhibitor action on the heart. Stimulation of the central end is followed by a fall in blood-pressure, frequently to a level below one-half the normal value; at the same time there is a diminution, brought about reflexly, in the rate of the heart-beat (Fig. 181). The fall in pressure, however, is due mainly to the dilatation of the arterioles, the result of an inhibition of the general vaso-reflex center, and partly to the diminution in the rate and force of the heart, the result of a simultaneous stimulation of the inhibitor center. This latter factor is of less importance than the former for the fall of pressure occurs equally well after division of all the cardiac nerves. For this reason the nerve was termed the depressor nerve of the vaso-motor center.

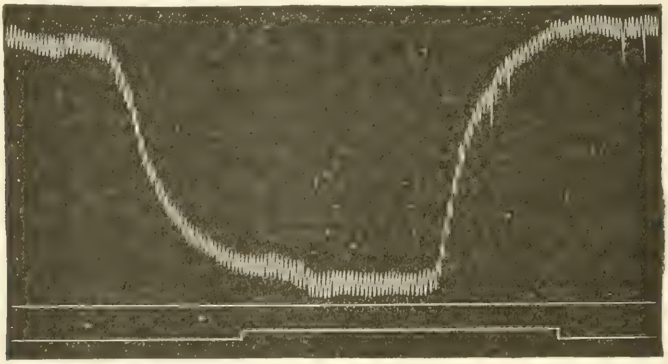

FIG. 181.—FALL OF BLOOD-PRESSURE FROM EXCITATION OF THE DEPRESSOR NERVE. The cylinder was stopped in the middle of the curve and the excitation maintained for seventeen minutes. The line of zero pressure (0,0) should be 30 mm. lower than here shown.—(*Bayliss*.)

On exposure of the abdominal cavity, it is observed during stimulation of the depressor that there is a notable dilatation of the intestinal vessels.

From this fact it was assumed that the action of the depressor nerve was to lower the general pressure through reflex dilatation of these vessels. It has been shown by Porter and Beyer that if the splanchnics are divided and the peripheral end stimulated so as to maintain the tonus of the intestinal vessels, and hence the general pressure, stimulation of the depressor nerve will nevertheless be followed by a fall of the blood-pressure almost as great as when the splanchnics are intact. From this it is evident that the depressor nerve is related to centers which influence the vascular apparatus in its entirety. It has been supposed that through it the heart can protect itself from injurious results of an excessive rise of arterial pressure.

Thus, when the intra-cardiac pressure or the intra-aortic pressure rises beyond a normal amount from increased resistance, the peripheral terminations of this nerve are stimulated with the result that the vaso-motor center is inhibited and the arterioles relaxed. Through this means the pressure falls and the work of the heart is lessened.

The Traube-Hering Waves.—Under certain experimental conditions the arterial blood-pressure tracing exhibits, in addition to the usual respiratory variations, certain longer rhythmic variations more or less wave-like in character, which are known as Traube-Hering waves. They can be developed on a blood-pressure tracing by injecting magnesium sulphate or morphine into the circulation, by tying the cerebral arteries, etc. These waves indicate a periodic contraction and dilatation of the blood-vessels, the result of a periodic stimulation of the vaso-motor center.

CHAPTER XV

RESPIRATION

Respiration is a process by which oxygen is introduced into, and carbon dioxid removed from, the body. The assimilation of the former and the evolution of the latter take place in the tissues as a part of the general process of nutrition. Without a constant supply of oxygen and an equally constant removal of the carbon dioxid, those chemic changes which underlie and condition all life phenomena could not be maintained.

The general process of respiration may be considered under the following headings, viz.:

1. The anatomy and general arrangement of the respiratory apparatus.
2. The mechanic movements of the thorax by which an interchange of atmospheric and intra-pulmonary air is accomplished.
3. The chemistry of respiration; the changes in composition undergone by the air, blood, and tissues.
4. The nerve mechanism by which the respiratory movements are maintained and coördinated.

THE RESPIRATORY APPARATUS

The respiratory apparatus consists essentially of:

1. The lungs and the air-passages leading into them: viz., the nasal chambers, mouth, pharynx, larynx, and trachea.
2. The thorax and its associated structures.

The Nasal Chambers.—The nasal chambers are the natural entrances for the inspired air. Their complicated structure slightly retards the movement of the air, in consequence of which its temperature and moisture are adjusted to the physiologic conditions of the lower respiratory passages. The mouth, though frequently serving as an entrance for air, is not primarily a respiratory passage. Both the nasal chambers and the mouth communicate posteriorly with the pharynx, in which the respiratory and the deglutitory passages cross each other, the former leading directly into the larynx.

The Larynx.—The larynx is a complicated mechanism serving the widely different though related functions of respiration and phonation. It consists of a framework of cartilages, articulating one with another, united by ligaments and capable of being moved, one on the other, by the action of muscles; it is covered externally with fibrous tissue and lined with mucous membrane. The superior laryngeal aperature is triangular in shape, the base being directed upward and slightly forward, the apex downward and backward. The inclination of the laryngeal aperature is almost vertical.

The cavity of the larynx is partially subdivided by the interposition of the vocal bands into a superior and an inferior portion. The opening, bounded by the vocal bands, is also triangular in shape, though in this case the base is directed backward, and the apex forward. (See chapter on Voice and Speech.)

The introduction of the vocal bands narrows at this level the air-passage and to some extent interferes with the free entrance of air. According to the investigations of Semon, the area of the air-passage above and below the phonatory apparatus is about 200 sq. mm.; while the area bounded by the vocal apparatus is but 155 sq. mm. during quiet respiration.

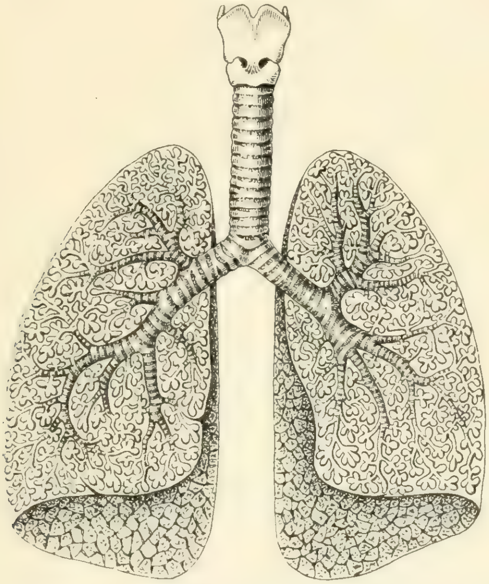

FIG. 182.—Human larynx, trachea, bronchi, and lungs; showing the ramification of the bronchi, and the division of the lungs into lobules.

The Trachea.—The trachea is a tube, some 12 centimeters in length, from two to two and a half centimeters in breadth, extending from the lower border of the larynx to a point opposite the fifth thoracic vertebra. It consists of an external fibrous and an internal mucous membrane, between which is a series of superposed **C**-shaped arches or rings of elastic cartilage, some 18 or 20 in number. Between the fibrous and mucous coats posteriorly, and occupying the space between and attached to the free ends of the cartilages, there is a layer of transversely arranged non-striated muscle-fibers, known as the *tracheal* muscle. The alternate contraction and relaxation of this muscle would by varying the distance between the ends of the cartilages, either diminish or increase the caliber of the trachea. The surface of the mucous membrane is covered by a layer of stratified columnar ciliated epithelium. In the submucous tissue there are a number of glands the ducts of which open on the free surface.

Opposite the fifth thoracic vertebra the trachea divides into a right and a left bronchus. Each bronchus again subdivides into two or three branches, which penetrate the corresponding lung.

The Lungs.—The lungs, in the physiologic condition, occupy the greater part of the cavity of the thorax. They are separated from each other by the contents of the mediastinal space: viz., the heart, the large blood-vessels, the esophagus, etc. Each lung is somewhat pyramidal in shape with the apex directed upward. The outer surface is convex and corresponds to the general conformation of the thorax. The inner surface is concave and accommodates the contents of the mediastinal space. The under surface of the lung is concave and rests on the diaphragm. The posterior border is convex; the anterior border is thin. At about the middle of the inner surface of the lung the blood-vessels which connect the heart with the interior of the lung enter and leave in company with the branches of the bronchi, bronchial arteries, veins, nerves, and lymphatics.

A histologic analysis of the lung shows it to consist of the branches of the bronchi, their subdivisions and ultimate terminations, blood-vessels, lymphatics and nerves, imbedded in a stroma of fibrous and elastic tissue. The anatomic relations which these structures bear one to another is as follows:—

Within the substance of the lung the bronchi divide and subdivide, giving origin to a large number of smaller branches, *the bronchial tubes*, which penetrate the lung in all directions. With this repeated subdivision the tubes become narrower, their walls thinner, their structure simpler. In passing from the larger to the smaller tubes the cartilaginous arches become shorter and thinner, and finally are represented by small angular and irregularly disposed plates. In the smallest tubes the cartilage entirely disappears. With the diminution of the caliber of the tube and a decrease in the thickness of its walls, there appears a layer of non-striated muscle-fibers, the so-called *bronchial muscle*, between the mucous and submucous tissues, which completely surrounds the tube and becomes especially well developed in those tubes devoid of cartilage. The fibrous and mucous coats at the same time diminish in thickness.

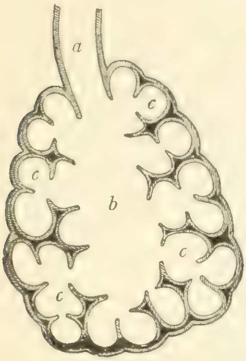

Fig. 183.—Single Lobule of Human Lung. *a*. Alveolar passage. *b*. Cavity of lobule or infundibulum. *c*. Pulmonary sacs. —(*Dalton*.)

Bronchial Innervation.—The bronchial muscles are presumably in a state of tonic contraction and impart to the bronchial tubes a certain average caliber best adapted for respiratory purposes. Experimental investigations indicate that they are innervated by efferent fibers of the vagus nerve (bronchoconstrictors and possibly broncho-dilatators) inasmuch as stimulation of this nerve is usually followed by a contraction of the muscles and a narrowing of the lumen of the bronchial system. These muscles may also be thrown into increased activity by the inhalation of irritating gases and into a tetanus by pathologic causes as seen in the various forms of asthma.

When the bronchial tube has been reduced to the diameter of about one millimeter, it is known as a *bronchiole* or a *terminal bronchus*. From the sides of the terminal bronchus and from its final termination there is given off a series of short branches which soon expand to form *lobules* or *alveoli*. The cavity of the alveolus is termed the infundibulum. From the inner surface of the alveolus and of the passageway leading into it, there project thin partitions which subdivide the outer portion of the general cavity or infundibulum into small spaces, the so-called air-sacs or air-cells (Fig. 183). The wall of the alveolus is extremely thin and consists of fibro-elastic tissue, supporting a very elaborate capillary network of blood-vessels. The bronchial system as far as the alveolar passages is lined by ciliated epithelium. The air-sacs are lined by flat epithelial plates of irregular shape, termed the *respiratory epithelium.* The alveoli are united one to another by fibro-elastic tissue.

The bronchial arteries which supply nutritive material to the pulmonary structures arise from the aorta as a rule, though sometimes from an intercostal artery. Each lung receives two arteries which accompany the bronchi as far as the distal ends of the alveolar passages. From the capillary network formed out of the terminals of these arteries, two systems of veins arise, one of which returns the blood from the larger tubes and empties it into the azygos vein; the other of which returns the blood from the smaller tubes and the alveolar passages, and empties it into the pulmonic veins. The blood in the pulmonic veins, though largely arterialized, nevertheless contains some venous blood derived from the veins arising from the capillary network of the bronchial arterioles.

The nerves distributed to the muscle-fibers of the bronchial arteries, and of the bronchial tubes and to the mucous membrane, are derived from the vagus and the sympathetic and enter the substance of the lung at and around its root.

In consequence of the presence of the elastic tissue, the lungs are distensible and elastic. After removal from the body the elastic tissue at once recoils, forcing out a portion of the contained air. The condition of the lung is now one of collapse. Under pressure, however, the lung can be readily distended or inflated. These properties endure for a long period after death, if not indefinitely, if the lungs are properly preserved. The capacity of the lungs can be made to vary within rather wide limits in virtue of the presence of the elastic tissue.

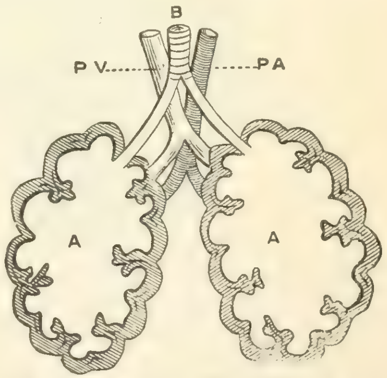

FIG. 184.—THE RELATION OF THE PULMONIC ARTERY, PA, AND THE PULMONIC VEIN, PV, TO THE LOBULES, AA. B. THE BRONCHIOLE.

The Pulmonic Blood-vessels.—The pulmonic artery which conducts the venous blood from the heart to the lungs divides beneath the arch of the aorta into a right and a left branch. Each branch with its subdivisions enters the lung at the hilum in company with the larger divisions of the bronchi. Within the lung the arteries divide and subdivide in a manner corresponding to that of the bronchial tubes, which they follow to their ultimate terminations. As the pulmonic lobules are approached, a small arterial branch plunges into the wall of the lobule (Fig. 184), in which it forms an elaborate capillary network which surrounds and embraces the air-sacs on all sides. As this network is to subserve the respiratory exchange of gases it lies nearer the inner than the outer surface of the lobule and in close relation to the respiratory epithelium. The air and blood are thus brought into intimate relationship, being separated only by the respiratory epithelium and the wall of the capillary vessel. The blood emerging from the capillary vessels is conducted by a corresponding converging system of vessels, the pulmonic veins, out of the lungs and into the left auricle of the heart. The main function of the pulmonic apparatus and the pulmonic division of the circulatory apparatus is to afford a ready means for the exhalation of the carbon dioxid and the absorption of oxygen. In consequence of this exchange of gases the blood changes in color from dark bluish-red to scarlet red. The relations of the heart and its vessels to the lungs and bronchial tubes are shown in Fig. 184.

The Thorax.—The thorax, in which the respiratory organs and their associated structures are lodged, is conic in shape, though somewhat compressed from before backward. Its apex is directed upward, its base downward. The walls of the thorax are composed, first, of a bony framework or skeleton and, second, of muscles and fascia.

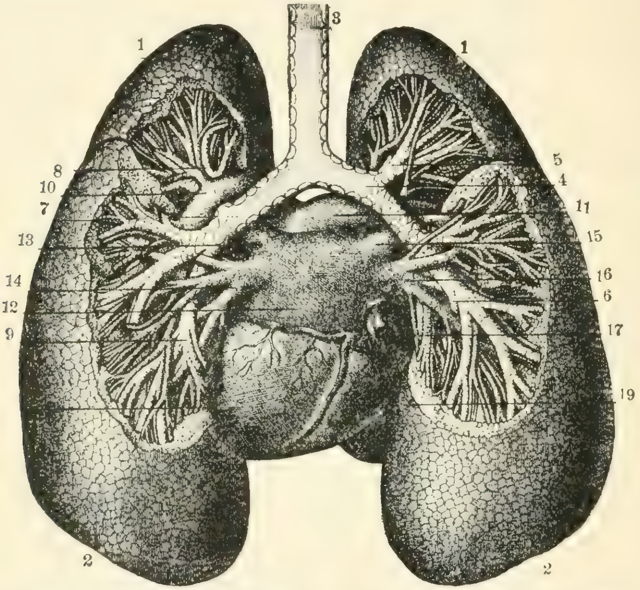

Fig. 185.—Bronchi and Lungs, Posterior View. 1, 1. Summit of lungs. 2, 2. Base of lungs. 3. Trachea. 4. Right bronchus. 5. Division to upper lobe of lung. 9. Division to lower lobe. 10. Left branch of pulmonic artery. 11. Right branch. 12. Left auricle of heart. 13. Left superior pulmonic vein. 14. Left inferior pulmonic vein. 15. Right superior pulmonic vein 16. Right inferior pulmonic vein. 17. Inferior vena cava. 18. Left ventrice of heart. 19. Right ventricle.—(*Sappey.*)

The bony framework is formed posteriorly by the thoracic vertebræ and the posterior extremities of the ribs, laterally by the ribs, and anteriorly by the costal cartilages and the sternum. The superior opening, through which pass the trachea, esophagus, and blood-vessels, is oval in outline and measures from side to side about 12.5 cm., and from before backward about 6.25 cm. The inferior opening is of large size, but irregular in its boundaries from the upward inclination of the ribs and the downward projection of the sternum.

The **ribs,** which form a large part of the thoracic walls, constitute a series of bony arches attached posteriorly to the vertebræ and anteriorly to the sternum through the intermediation of their cartilages. The last two form an exception. The ribs are somewhat twisted upon themselves and pursue an oblique direction from above downward and forward. As a result the anterior extremity lies at a lower level than the posterior. The costal cartilages are directed upward and forward, with the exception of the upper three, which are almost horizontal.

The costo-vertebral and costo-chondral and the chondro-sternal articulations are diarthrodial in character and endow the thoracic walls with a considerable degree of mobility. The costo-vertebral joints are two in number, the first being formed by the beveled head of the rib and the bodies of the two adjoining vertebræ; the second, by the tubercle of the rib and the transverse process. The costo-chondral and the chondro-sternal articulations, as their names imply, are formed by the ribs, cartilages, and sternum.

The **muscles** which complete the formation of the thoracic walls are as follows: the diaphram, the intercostales externi and interni, the levatores costarum, the triangularis sterni, and the infra-costales.

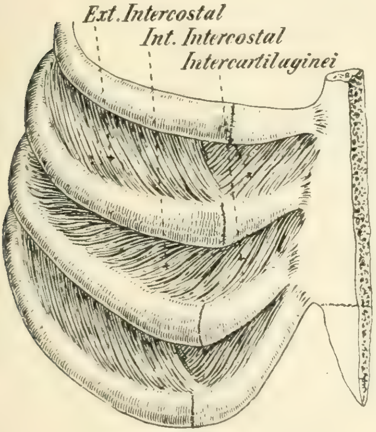

FIG. 186.—SHOWING THE SITUATION, THE POINTS OF ATTACHMENT, AND DIRECTION OF THE INTERCOSTAL MUSCLES. 1. The intercostales externi. 2. The intercostales interni. 3. The intercartilaginei.

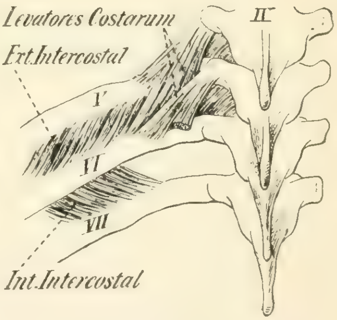

FIG. 187.—VIEW FROM BEHIND OF FOUR DORSAL VERTEBRÆ AND THREE ATTACHED RIBS, SHOWING THE ATTACHMENT OF THE ELEVATOR MUSCLES OF THE RIBS AND THE INTERCOSTALS.—(*After Allen Thomson.*)

The **diaphragm** is the musculo-membranous sheet which closes the inferior opening of the thorax and completely separates its cavity from that of the abdomen. It consists of two muscles which arise from the bodies of the first three or four lumbar vertebræ and neighboring fascia, from the border of the six lower ribs, and from the ensiform cartilage. From this extensive origin the muscle-fibers pass centrally to be inserted into a common tendon. As the direction of the fibers is from below upward and inward, the diaphragm is somewhat dome-shaped. Its inferior border is for a short distance in contact with the sides of the thorax.

The *intercostales externi*, eleven in number on each side, occupy the spaces between the ribs to which they are attached from the tubercle to the anterior extremity (Figs. 186 and 187). Their fibers, which are arranged in parallel bundles, are directed from above downward and from behind forward. The point of attachment, therefore, of any given bundle of fibers to the rib above, lies nearer the vertebral column, nearer the fulcrum, than the point of attachment below.

The *intercostales interni*, eleven in number, occupy the spaces between, and are attached to the ribs from the tubercle to the anterior extremity of the cartilages. Their fibers, which are also arranged in parallel bundles, are directed from above downward and backward (Figs. 186 and 187). The portions of the internal intercostals between the cartilages are frequently termed *intercartilaginei*.

The *levatores costarum* are twelve in number on either side. They arise from the tips of the transverse processes of the last cervical and the thoracic vertebræ with the exception of the last. From the point of origin the fibers pass downward and outward in a diverging manner to be inserted into the ribs between the tubercle and the angle. Their action, as their name implies, is to elevate the posterior portion of the ribs.

The *triangularis sterni* arises from the side of the posterior surface of the lower third of the sternum and is inserted by fleshy slips into the cartilages of the ribs from the second to the sixth.

From the fact that the inferior opening of the thorax as well as the intercostal spaces are completely closed by the foregoing muscles, and from the further fact that the superior is closed by fascia except at those points through which pass the trachea, blood-vessels and esophagus, the cavity of the thorax is absolutely air-tight.

The Pleuræ.—Each lung is surrounded by a closed invaginated serous sac, the pleura, of which the inner portion is reflected over and is closely adherent to the surface of the entire lung as far as its root; the outer portion is reflected over the inner wall of the thorax, the superior surface of the diaphragm, and the viscera of the mediastinum. Under normal conditions these two layers of the pleura, the pulmonic and parietal or thoracic are in contact, or at most separated only by a thin capillary layer of lymph. The presence of this fluid prevents appreciable friction as the two surfaces play against each other in consequence of the movement of the lungs.

THE MECHANIC MOVEMENTS OF THE THORAX

As the blood flows through the pulmonic capillaries it yields carbon dioxid to, and receives oxygen from, the air in the pulmonic alveoli. As a result, the intra-pulmonic air changes in composition which interferes to a greater or less extent with the further exchange of gases. That this exchange may continue, it is of primary importance that the air within the alveoli be renewed as rapidly as it is vitiated. This is accomplished by an alternate increase and decrease in the capacity of the thorax, accompanied by corresponding changes in the capacity of the lungs. During the former there is an inflow of atmospheric air (inspiration), during the latter an outflow of intra-pulmonic air (expiration). The continuous recurrence of these two movements brings about that degree of pulmonic ventilation necessary to the normal exchange of gases between the blood and the air. The two movements together constitute a respiratory act or cycle.

In the course of the respiratory cycles the thorax presents alternately a short period of rest—viz.: between the end of an expiration and the beginning of an inspiration—and a relatively long period of activity, including both inspiration and expiration. The former may be regarded as the static, the latter as the dynamic condition of the thorax. In the static condition, the thorax and its contained and associated organs sustain a definite relation one to another; in the dynamic conditions these relations undergo a change the extent of which is proportional to the extent of the movements.[1]

THE STATIC CONDITION

Relation of the Thoracic Organs.—Intra-pulmonic Pressure: Intra-thoracic Pressure.—In the *static* condition of the thorax the lungs, by virtue of their distensibility, completely fill all parts of the thorax not occupied by the heart and great blood-vessels (Fig. 188). This condition is maintained by the pressure of the air within the lungs, the *intra-pulmonic pressure*, which with the respiratory passages open, is that of the atmosphere, 760 mm. Hg. This relation persists so long as the thorax remains air-tight. If the skin and muscles covering an intercostal space be removed the lung can be seen in close contact with the parietal layer of the pleura gliding by with each inspiration and expiration. If, however, an opening be now made in the pleura sufficient to admit air, the lung immediately collapses and a pleural cavity is established. A pleural cavity, therefore, does not exist in physiological conditions, it is potential only. The pressure of air within and without the lung counterbalancing, at the moment the air is admitted, the elastic tissue at once recoils and forces a large part of the air out of the lung. This is a proof that in the normal condition, the lungs, distended by atmospheric pressure from within, are in a state of elastic tension and ever endeavoring to pull the pulmonic layer of the pleura away from the parietal layer. That they do not succeed in doing so is due to the fact that the atmospheric pressure from without is prevented from acting on the lung by the firm unyielding walls of the thorax.

Intra-thoracic Pressure.—As a result of the elastic tension of the lungs a fractional part of the intra-pulmonic pressure, 760 mm. Hg., is counterbalanced or opposed, so that the heart and great vessels and other intra-thoracic viscera are subjected to a pressure somewhat less than that of the atmosphere; the amount of this pressure will be that of the atmosphere *less* that exerted by the elastic tissue of the lung in the opposite direction, expressed in terms of millimeters of mercury. In the thorax but outside the lungs, there then prevails a pressure, negative to the pressure inside the lungs and which is known as the *intra-thoracic pressure.*

The amount of this intra-thoracic pressure can be approximately determined in several ways. Thus, if shortly after death a mercurial manometer be inserted air-tight into the trachea of a human being and the thorax opened, the lungs will recoil and compress their contained air. The mercurial manometer will at once show an excess of pressure in the trachea of about

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[1] It is a matter of discussion as to whether or not there is an absolute cessation of movement of the thoracic walls at the end of expiration. A graphic record of the movement shows that if there is no absolute cessation, the movement is so slight that, for the purposes here intended, a pause may be admitted. With this admission it is, however, recognized that the forces, both elastic and muscular, which are always acting on the thoracic walls, though in opposite directions, have not ceased to act, but have become so nearly equal that for a brief period they are practically in a condition of equilibrium, during which the thoracic walls are stationary.

6 mm. This was taken by Donders as a measure of the force with which the lungs endeavor to recoil. The intra-thoracic pressure would be, therefore, atmospheric pressure, 760 mm., less 6 mm., or 754 mm. Hg. Another method is to insert a rubber catheter through a small opening in an intercostal space into the thoracic cavity. The air which enters through the open extremities of the catheter and leads to a collapse of the lungs may be subsequently aspirated, when the lung returns to its normal position. The catheter is then placed in connection with a water manometer. On establishing a communication between them, by the turning of a stopcock, the water will rise in the proximal and fall in the distal limb of the manometer, indicating a pressure in the thorax *negative* to that in the lung. The difference in the level of the water in the two limbs of the manometer, expressed in millimeters of mercury, would also represent the force with which the elastic tissue strives to recoil, and the extent to which it opposes the atmospheric pressure. This subtracted from the atmospheric pressure would give the intra-thoracic pressure. In the living dog this latter is less than the former, to the extent of from 3.5 to 5.5 mm. For the same reason the superior surface of the diaphragm also experiences a pressure less than that of the atmosphere. Owing to the soft and yielding character of the abdominal walls the atmospheric pressure is transmitted through the abdominal organs to the inferior surface of the diaphragm. The pressure being greater from below than above, the diaphragm is forced upward until it assumes the dome-like appearance it usually presents. (These relations are shown in Fig. 188.)

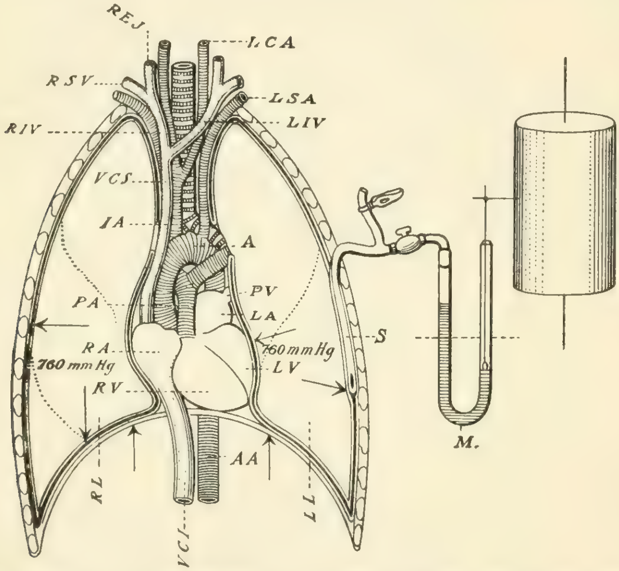


FIG. 188.—SECTION OF THORAX WITH THE LUNGS, HEART, AND PRINCIPAL VESSELS. *S.* Catheter introduced into the pleural space and connected with a manometer.—(*After Morat and Doyen.*)

The cause of the negativity of the intra-thoracic pressure is connected with the change in the relation of the lungs to the thorax attending the first inspiration. Previous to birth the walls of the alveoli and bronchioles are collapsed and in apposition. The larger bronchial tubes in all probability contain fluid. The lungs therefore are devoid of air (atelectatic), and, having a specific gravity greater than water, readily sink when placed in this fluid. The capacity of the thorax does not exceed the volume of the lungs. With the first inspiration, however, the thoracic walls take a new position. The air at once rushes into the lungs and distends them. But as the capacity of the thorax even at the end of the expiration is now greater than the volume which the lungs would assume unless distended, there at once arises the elastic recoil in the opposite direction, the condition which gives rise to the negativity of the pressure in the thoracic cavity. It is also probable that as the child develops, the thorax grows more rapidly than the lungs, giving rise to a condition which would increase and accentuate the elastic tension and thus increase the negativity of the intra-thoracic pressure.

THE DYNAMIC CONDITION

In the *dynamic* condition, the thorax and its contained organs undergo a series of movements in consequence of which the relations among them characteristic of the static condition, are temporarily changed. To these movements the term respiratory has been given, as a result of which, the ventilation of the lungs is accomplished.

The Respiratory Movements.—The respiratory movements consist of an alternate increase and decrease in the capacity of the thorax, accompanied by corresponding changes in the capacity of the lungs, the two movements being known as *inspiration* and *expiration* respectively. During the increase in the thoracic capacity, the air passively flows into the lungs; during the decrease in the thoracic capacity, the air passively flows out of the lungs. In both movements the lungs play an entirely passive part, their movements being determined by the pressure of air within them and by the outward movement of the thoracic walls, with which they are in close contact.

1. **Inspiration** is an active process, the result of muscle activity.
2. **Expiration** is a passive process, the result mainly of the recoil of the elastic tissue of the walls of the thorax and abdomen and of the elastic tissue of the lungs.

In inspiration the thorax is enlarged in all its diameters: viz., vertical, transverse, and antero-posterior. In expiration the thorax is diminished in all its diameters as it returns to its former condition.

Inspiratory Muscles.—The muscles which from their origin, direction, and insertion contribute to the enlargement or expansion of the thorax are quite numerous, and include those muscles which enter into the formation of the thoracic walls (intrinsic muscles), as well as certain muscles which, having their origin elsewhere, are attached to the thoracic walls at different points (extrinsic muscles), though the extent to which they are called into activity depends on the necessity for either tranquil or energetic inspirations. The gradations between a minimum and a maximum inspiration are very slight, and it is difficult to state at what particular instant any given muscle begins to act. It is customary, however, to divide the muscles into two groups: (1) Those active in the average or ordinary inspirations, and (2) those active in maximum or extraordinary inspirations. Among the muscles active in ordinary inspirations may be mentioned the *diaphragm*, the *intercostales externi*, the *intercartilaginei*, the *levatores costarum*, the *scaleni*, and the *ser-*

ratus posticus superior. Among the muscles active in extraordinary inspirations may be mentioned, in addition to the foregoing, the *sterno-cleido-mastoideus*, the *trapezius*, and the *pectorales minor* and *major.*

The *vertical* diameter is increased by the contraction and descent of the *diaphragm*, and more especially of its lateral muscular portions. At the end of an expiration the diaphragm is relaxed, and the lower portion closely applied to the walls of the thorax. At the beginning of an inspiration the muscle-fibers contract, shorten, and approximate a straight line, whereby not only is the convexity of the diaphragm diminished, but that portion in contact with the thorax is drawn away, thus making a large free space triangular in shape, termed the complementary pleural space, into which the lateral and posterior portions of the lungs at once descend. The attachment of the central tendon of the diaphragm to the pericardium prevents any marked descent of this portion except in forcible inspiratory efforts. The vertical diameters are thus enlarged, though unequally in different regions of the thorax.

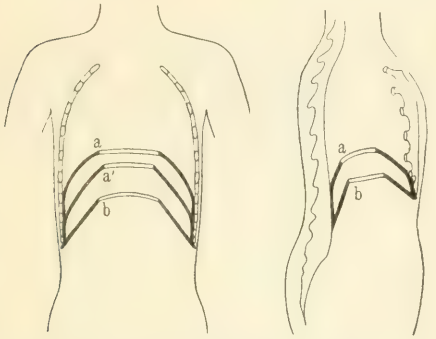


Fig. 189.—Diagram Showing the Position and Shape of the Diaphragm at Rest *a* and During Inspiration *a'* and *b*.—(*Boruttau.*)

As the diaphragm descends it displaces the abdominal viscera, forcing them downward against the abdominal walls, which advance and become more convex. In forcible inspiration the diaphragm, acting from the central tendon as the more fixed point, would draw the lower portion of the thorax inward were this not prevented by the outward pressure of the displaced viscera.

Coincidently with the descent of the diaphragm and the partial removal of the pressure on the under surface of the lung, the intra-pulmonic air expands. As it expands it distends the lungs in the vertical direction, causing them to follow the diaphragm and to occupy the so-called complementary pleural space. With the expansion of the intra-pulmonic air there is a fall in its pressure below the atmospheric pressure, to be followed immediately by an inflow of air until atmospheric pressure is again established. This occurs at the end of the inspiration.

The *antero-posterior* and *transverse* diameters are increased by the elevation and outward rotation of the ribs and an advance of the sternum, both movements made possible by the construction and arrangement of the costo-vertebral and costo-chondral and chondro-sternal articulations. The construction of these articulations is such as to permit at the first a slight elevation and depression of the head of the rib, and at the second a gliding of the tubercle on the transverse process. The axis around which the rib rotates practically coincides with the axis of the rib neck, which in the upper part of the thorax is almost horizontal, in the lower part somewhat sagittal in direction. Hence when the ribs are elevated the upper part of the thorax increases in its antero-posterior, the lower part in its transverse diameters. At the same time, the lower portion of the sternum is pushed forward and upward by the elevation of the anterior extremity of the ribs and the widening of the angle of the costo-chondral articulation. With the elevation of the ribs there goes an eversion or outward rotation which still further increases the transverse diameters. Coincidently with the increase in the transverse and antero-posterior diameters of the thorax, and the partial removal of the pressure on the lateral surfaces of the lungs there is also an additional expansion of the intra-pulmonic air. As it expands it distends the lungs, causing them to occupy the available space thus established. With the expansion of the intra-pulmonic air there is a still further fall of pressure and an additional inrush of air. Between the descent of the diaphragm and the elevation of the ribs and the advance of the sternum the volume of air necessary for the ordinary respiratory needs is introduced into the lungs.

This elevation and outward rotation of the ribs is the resultant of the coöperation of the following muscles, viz.: the *intercostales externi*, the *intercartilaginei*, the *levatores costarum*, the *scaleni* and the *serratus posticus superior*.

The action of the *external intercostal* muscles, as well as the action of the *intercartilaginei muscles*, has been a subject of much discussion. Some investigators have maintained that they are elevators of the ribs, and therefore inspiratory; others that they are depressors of the ribs, and therefore expiratory in function. At the present time the general consensus of opinion is that the former view is the one most in accordance with the facts. In the following explanation as to their action, their relation to the ribs and to the cartilages, must be recalled to mind. The relation of the external intercostals is such that the point of attachment of any given bundle of fibers to the rib above lies nearer the vertebral column, nearer the fulcrum, than the point of attachment to the rib below. The relation of the intercartilaginei to the cartilages is such that the point of attachment of any given bundle of fibers to the cartilage above lies nearer the sternum, nearer the fulcrum, than the point of attachment to the cartilage below. The situation of the muscles and the shortness of their fibers render it extremely difficult to obtain myographic tracings which would elucidate their action in elevating the ribs and cartilages.

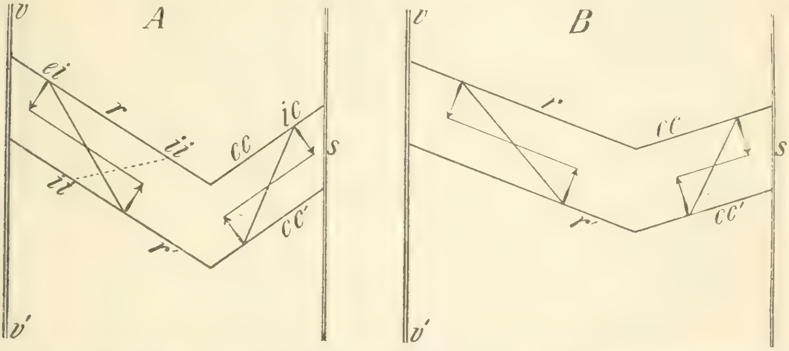


FIG. 190.—DIAGRAMS ILLUSTRATING THE ACTION OF THE EXTERNAL INTERCOSTAL AND INTERCARTILAGINEI MUSCLES.

A clear conception of their action, however, may be arrived at by the study of the schematic model first presented by Hamberger. Fig. 190. In this model v–v' is a vertical support carrying two freely movable parallel bars $r\ r'$, united at their opposite ends with two other freely movable and parallel bars cc, cc' carried by a second vertical support, s, representing respectively the vertebral column, two adjoining ribs, two adjacent cartilages, and the sternum. Diagram A shows the position of the different parts at the end of expiration and B their position at the end of inspiration. The parallel bars are joined to each other by elastic bands *ei* and *ic* having the direction of and representing the external intercostal and intercartilaginei muscles, respectively. The bars are depressed to sufficiently elongate and tense the elastic bands and thus imitate the condition of the muscles in so far as tension is concerned prior to their contraction. On releasing the bars the elastic bands at once recoil and the bars representing ribs and cartilages are raised. Although the elastic forces, acting in opposite directions as indicated by the arrows are equal, the bars are yet raised for the reason that in accordance with the parallelogram of forces, the components acting upward on the long arms of the levers preponderate over the components acting downward on the short arms of the levers. This, taken in connection with the fact that the distances between the adjoining bars are fixed, leads not only to an elevation of the bars, but to a widening of the angle between them and an advance of the second vertical support. The actions of these bands thus disclose and illustrate the actions of both the external intercostal and intercartilaginei muscles. It must therefore be concluded that these muscles are the elevators of the ribs and cartilages and hence, inspiratory in function. Of late the correctness of Hamberger's view has been confirmed by experiments on living animals.

The *levatores costarum*, as is evident from their points of origin and insertion, elevate the ribs posteriorly.

The *scalenus* muscles, *anticus*, *medius*, and *posticus*, arise from the transverse processes of the cervical vertebræ, and after pursuing a downward and forward direction are inserted into the sternal end of the first and second ribs. The action of the first two, at least, is to elevate the first rib and thus establish a fixed point from which the intercostal muscles can act. The posticus has doubtless a similar action on the second rib.

The *serratus posticus superior*, a quadrilateral sheet of muscle-fibers, arises mainly from the spines of the last cervical and first and second thoracic vertebræ. The anterior extremity is serrated and attached to the outer surfaces of the second, third, fourth, and fifth ribs beyond the angle. The action of the muscle is the elevation of the ribs to which it is attached.

Forced Inspiration.—In *forced* or *extraordinary* inspirations, whereby the capacity of the thorax is still further increased, the foregoing muscles are reinforced by the *sterno-cleido-mastoideus*, the *trapezius*, and the *pectorales minor* and *major*. Their functions will become apparent from a consideration of their origins and insertions.

Expiratory Forces and Muscles.—Expiration, as previously stated, is a passive process brought about by the recoil of the elastic tissues of the thoracic and abdominal walls, and of the lungs, all of which have been stretched and made tense during inspiration. With the cessation of the inspiratory effort the elastic forces, assisted by the weight of the ribs, sternum, and soft tissues, return the thorax to its former condition. The result is a diminution of all the diameters of the thorax. The *vertical* diameter is diminished by the recoil of the tense abdominal walls, the replacement of the abdominal organs and the consequent ascent of the diaphragm to its former position. The *transverse* and *antero-posterior* diameters are diminished by the descent of the ribs, sternum, and lungs. Coincident with the return of the thoracic walls to their former condition there is a recoil of the elastic tissue of the lungs, in consequence of which there is a compression of the intra-pulmonic air. With its compression there is a rise of pressure above atmospheric and at once there is an outflow of intra-pulmonic air until atmospheric pressure is again established at the end of expiration.

It is somewhat uncertain if a normal expiratory movement necessitates active muscle contraction. If, however, there is any impairment of the elasticity of the lungs or ribs, or any interference with the free exit of the intra-pulmonic air, it is highly probable that the elastic forces are assisted by the internal intercostal and triangularis sterni muscles. It has been insisted upon also that while the recoil of the elastic tissues is effective in the early stages of an expiration, it is ineffective in the later stages. Hence there arises a necessity for muscle assistance.

The action of the *internal intercostals* is less clearly understood than that of the external intercostals. If, however, the *direction* of these muscles as indicated in Fig. 190, diagram *A*, by the dotted line *ii, ii*, be considered it would seem that their action would be the opposite of that of the external intercostals—that is, it would be to depress the ribs. Employing the Hamberger model to elucidate the functions of these muscles it is apparent that if the elastic band, *ii, ii*, recoils, the elastic force of the two halves, though equal, will act in opposite directions, but as the component acting on the long arm of the level preponderates over that acting on the short arm of the lever, the ribs will be depressed. The action of the band is supposed to disclose and illustrate the action of the muscle. If this is the case the internal intercostal muscles must therefore be expiratory in function.

The *triangularis sterni* muscle, judging from its anatomic relations, in all probability assists in expiration by depressing the cartilages to which it is attached and as a further result depressing the anterior extremities of the ribs.

Forced Expiration.—After the elastic forces have ceased to act and the normal expiratory movement has been brought to a close, the thorax can be, to a considerable extent, still further diminished in all its diameters by the contraction, through volitional effort, of abdominal and thoracic muscles. To this decrease in the capacity of the thorax, as a result of which a much larger volume of air is expelled from the lungs than during passive expiration, the term *forced* expiration has been given. With the cessation of muscle activity the elastic forces of the now-compressed thoracic walls, aided by the return of the upwardly displaced abdominal organs, at once restore the thoracic walls to the position they had attained at the end of passive expiration. Of the muscles active in *forced* expiration in addition to the intercostales interni and the triangularis sterni, the following may be mentioned, viz.: the *abdominales*, the *serratus posticus inferior*, and the *quadratus lumborum*.

The conjoint action of these muscles is to diminish the convexity of the abdominal walls and to exert a pressure on the abdominal organs. These, taking the line of least resistance, are forced upward against the inferior surface of the diaphragm, which in consequence becomes more strongly curved and ascends higher into the thorax. The vertical diameter of the thorax is thus diminished. Acting from the pelvis as a fixed point, these muscles will also draw downward and inward the lower end of the sternum and the lower ribs and diminish the antero-posterior and transverse diameters.

Movements of the Lungs.—As the thorax is enlarging in all its diameters during inspiration, through muscle activity, the lungs are correspondingly enlarging in all their diameters, by virtue of their distensibility, through the pressure of the air within them. The lungs must therefore move downward, outward and forward. That this is the case is made evident both by an examination of the lungs through an intercostal space after removal of the skin and intercostal muscles, and by the methods of percussion. The inferior border of each lung descends from the lower border of the sixth to the eleventh rib, inserting itself into the space developed between the thorax and diaphragm as the latter contracts and is drawn away from the former. In consequence of the lateral expansion the anterior border of each lung advances toward the middle line until the heart is almost covered. With the beginning and continuance of expiration the lungs exhibit a reverse movement which continues until they reach their original position. At all times, however, the movements of the lungs are entirely passive and determined by the movements of the thorax.

The Changes in the Relation of the Thoracic Organs, and in the Intra-pulmonic and Intra-thoracic Pressures.—In the *dynamic* condition, as previously stated, the relations of the thoracic organs undergo a change as well as the intra-pulmonic and intra-thoracic pressures. Thus during inspiration the diaphragm descends, the ribs ascend and outwardly rotate and the sternum advances, the result of which is an enlargement in the diameters of the thorax. Coincidently with the enlargement of the thorax through muscle activity there goes a corresponding increase in the size and capacity of the lungs, in consequence of the expansion and pressure of the air in the pulmonary alveoli.

During expiration the diaphragm ascends in consequence of the return of the displaced abdominal viscera, the ribs descend and inwardly rotate and the sternum recedes from the recoil of the elastic tissues, the result of which is a diminution in the diameters of the thorax. Coincidently with the diminution of the thorax there goes a decrease in the size and capacity of the lungs in consequence of the recoil of their elastic tissue whereby the air in the lungs is compressed.

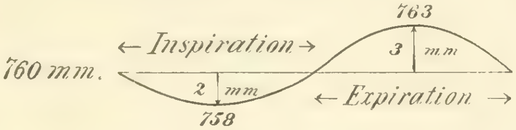
The *intra-pulmonic pressure* in consequence of the alternate expansion and compression of the intra-pulmonic air also undergoes a considerable variation.

During inspiration the intra-pulmonic air expands. With the expansion its pressure falls; but though it is now *less* than atmospheric pressure it is yet much greater than the opposing force of the lung tissue. As a result of the fall of intra-pulmonic pressure, there is a rapid inflow of air which continues until atmospheric pressure is restored; that is, at the end of the inspiration.

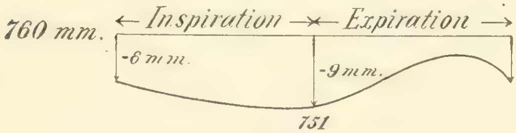
During expiration the intra-pulmonic air becomes compressed. With the compression its pressure rises above that of the atmosphere and in consequence there is a rapid outflow of air, which continues until atmospheric pressure is again restored; that is, at the end of the expiration. (Fig. 192, *A*.)

The cause for the fall of intra-pulmonic pressure during inspiration and the rise during expiration is to be found in the resistance offered by the air-passages to the movement of the air, throughout their entire extent, and especially at the level of the vocal bands. The greater the resistance, from whatever cause, physiologic or pathologic, the greater the variations of the pressure. If the inspiratory and expiratory movements take place slowly the intra-pulmonic pressure may scarcely vary in either direction.

In quiet inspiration the fall of pressure, as indicated by a manometer inserted into one nostril, seldom amounts to more than 1.5 mm. of Hg., the rise in expiration, 2.5 to 3 mm. of Hg. In forcible inspiratory and expiratory efforts these limits may be largely exceeded. Thus it was found by Donders that with one nostril closed and a mercurial manometer inserted into the other the pressure by voluntary efforts could be made to fall 57 mm. during inspiration and to rise 87 mm. during expiration. The changes in intra-pulmonic pressure are graphically represented in the upper half of Fig. 191.



A. Intra-pulmonic Pressures.



B. Intra-thoracic Pressure.

Fig. 191.—Representing the Changes, 1, in the Intra-pulmonic, and 2, in the Intra-thoracic Pressures during Inspiration and Expiration.

The *intra-thoracic pressure* also varies during both inspiration and expiration. As the thorax enlarges and the intra-pulmonic pressure falls, the recoil of the elastic tissue increases, with the result of still further diminishing the intra-thoracic pressure, until its maximum is reached near the end of the inspiration. The fall of intra-thoracic pressure at the end of a quiet inspiration reaches to about 9 mm. Hg. In forcible inspiratory efforts this fall in intra-thoracic pressure may amount to 30 or 40 mm. of Hg. As the thorax again diminishes and the intra-pulmonic pressure rises above the atmospheric pressure, the recoil of the elastic tissue is again opposed, with the result of increasing the intra-thoracic pressure, until the former condition of pressure has been regained at the end of the expiration. Neither the fall nor the subsequent rise of the intra-thoracic pressure takes place, however, in a steadily progressive manner for the following reasons: If a tracing were made of the variations in the circumference of the thorax during a respiratory movement it would resemble in its main features the tracing in Fig. 191, and variations in any linear dimension of the lung would be of course in the same proportion. This amount of elongation of elastic tissue in any direction would likewise be proportional to the force of elastic recoil. Therefore the intra-thoracic pressure would vary from a uniform decrease and increase just as the curve of Fig. 191 varies from uniform straight lines. The changes in intra-thoracic pressure are graphically represented in Fig. 191, *B*.

The intra-thoracic pressure and its variations influence favorably the flow of lymph through the thoracic duct (see page 225), as well as the flow of blood from the extra-thoracic veins into the intra-thoracic veins, the right side of the heart, and the cardio-pulmonary vessels. (See paragraphs at the end of this chapter.)

The succession of events in the thorax at the time of a respiratory act may be summarized as follows:

During Inspiration.

1. Enlargement of the thoracic diameters by muscle action.
2. Increase in the negativity of the intra-thoracic pressure.
3. Expansion of intra-pulmonic (alveolar) air.
4. Expansion of the lungs.
5. Lowering of the intra-pulmonic air pressure below the atmospheric air pressure.
6. Inflow of atmospheric air, in consequence of its higher pressure, until the intra-pulmonic air pressure rises to that of the atmosphere.

During Expiration.

1. Diminution of the thoracic diameters by the action of elastic forces.
2. Decrease in the negativity of the intra-thoracic pressure.
3. Recoil of the lungs.
4. Compression of the intra-pulmonic (alveolar) air.
5. Rise of intra-pulmonic air pressure above the atmospheric air pressure.
6. Outflow of intra-pulmonic air, in consequence of its higher pressure, until the intra-pulmonic air pressure falls to that of the atmosphere.

Respiratory Movements of the Upper Air-passages.—The resistance to the entrance of air into and through the respiratory tract is much diminished by respiratory movements of the nares and larynx which are associated and occur synchronously with the movement of the thorax.

The nares at each inspiration are dilated by the outward movement of their alæ or wings, the result of muscle activity. At each expiration they are diminished by the return of their cartilages through the play of elastic forces. The larynx, as shown by observation with the laryngoscope, exhibits corresponding movements of the vocal membranes. Their introduction at this level naturally narrows the tract, and would interfere with both the entrance and the exit of air were they not kept widely asunder during the time they are not required for purposes of phonation. This is accomplished by the tonic contraction of the posterior crico-arytenoid muscles, which are entirely respiratory in function.

It is not infrequently stated that these membranes exhibit considerable oscillations, outward and inward, corresponding to the movements of inspiration and expiration. The statements of the majority of laryngologists do not favor this view. During tranquil breathing the membranes are widely separated and almost stationary, seldom moving in either direction more than a few millimeters. In labored respirations these movements are naturally increased in extent. The irregular movements of the membranes occasioned by the unskilful use of the laryngoscope, especially with nervous patients, are not to be regarded as strictly physiologic. The respiratory space in quiet breathing is an isosceles triangle, with a length of 20 mm. and a width at the base of 15.5 mm. with an area of 155 mm.

Respiratory Types.—Observation of the respiratory movements in the two sexes shows that while the enlargement of the thoracic cavity is accomplished both by the descent of the diaphragm (as shown by the protrusion of the abdomen) and the elevation of the thoracic walls, the former movement preponderates in the male, the latter in the female, giving rise to what has been termed in the one case the *diaphragmatic* or *abdominal type* and in the other the *thoracic* or *costal type* of respiration. The cause of this greater mobility and activity of the thorax in the female has been a subject of much discussion. It has been attributed, on the one hand, to the necessity for a physiologic adjustment between respiration and child-bearing, and therefore a specific sex peculiarity; on the other hand, it has been attributed to persistent constriction of the waist, in consequence of which the full play of the diaphragm is prevented and the burden of inspiration is thrown on the thoracic muscles. It has been assumed that if inspiration were confined in women to the diaphragm, there would arise in the latter stages of gestation such an increase in intra-abdominal pressure that not only would respiratory exchanges be interfered with, but fetal life might be unfavorably influenced, if not endangered. Modern investigations have not confirmed this assumption, but, on the contrary, have corroborated the view that the preponderance of thoracic movement is due to the influences of dress restrictions, for with their removal the so-called costal type of breathing entirely disappears. While gestation may lead to a greater activity of the thorax, this is but temporary, for with its termination there is a return to the diaphragmatic type of breathing.

Number of Respirations per Minute.—The number of respirations which occur in a unit of time varies with a variety of conditions, the most important of which is age. The results of the observations of Quetelet on this point, which are generally accepted, are as follows:

Age.	Respirations per Minute.	Age.	Respirations per Minute.
0– 1 year	44	20–25 years	18.7
5 years	26	25–30 years	15.0
15–20 years	20	30–50 years	17.0

From these observations it may be assumed that the average number of respirations in the adult is eighteen per minute, though varying from moment to moment from sixteen to twenty. During sleep, however, the respiratory movements often diminish in number as much as 30 per cent., at the same time diminishing in depth.

Rhythm.—Each respiratory act takes place normally in a regular methodic manner, each event occurring in a definite sequence and occupying the same relative period of time. This rhythm, however, is not infrequently temporarily disturbed by emotions, volitional acts, muscle activity, phonation, changes in the composition of the blood, etc.; with the removal of these disturbing factors, the respiratory mechanism soon returns to its normal condition.

A graphic representation of the excursions of the thoracic walls, rhythmic or otherwise, is obtained by fastening to the thorax an apparatus, a *stethometer* or a *pneumograph*, which by means of a tambour takes up and transmits the movement to a second tambour provided with a recording lever. A simple form of pneumograph, suggested by Fitz (Fig. 192), consists of a coil of wire two and a half centimeters in diameter and about 40 centimeters in length, enclosed by thin rubber tubing, one end of which is closed, the other placed in communication either with a tambour and lever or with a piston recorder. By means of an inelastic cord or chain the apparatus is securely fastened to the chest. With each inspiration the spring is elongated, the air within the system is rarefied, and as a result the lever falls; with each expiration the reverse conditions obtain and the lever rises. If the lever be applied to the recording surface of a moving cylinder, a curve of the thoracic movement, a *pneumatogram*, is obtained (Fig. 193), from which it is apparent that inspiration takes place more abruptly and occupies a shorter period of time than expiration; that expiration immediately follows inspiration, but that there is a slight pause between the end of the expiration and the beginning of the inspiration. The time relations of the two movements can be obtained by a magnet-signal actuated by an electric current interrupted once a second. The ratio of inspiration to expiration has been represented as 5 to 6, or 6 to 8.

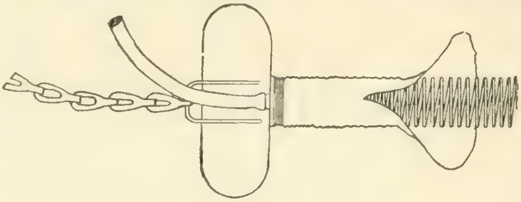


Fig. 192.—Pneumograph.—(*Fitz.*)

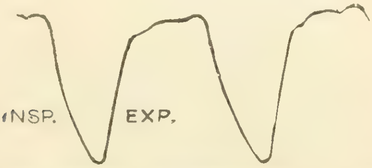


Fig. 193.—A Pneumatogram.—(*After Marey.*)

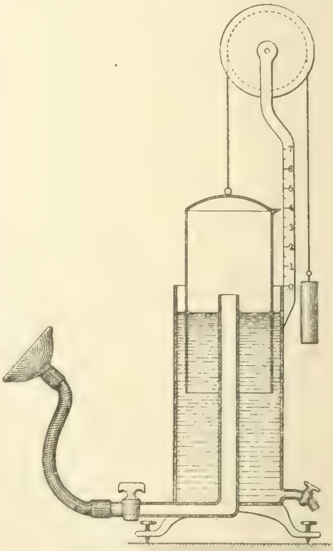


Fig. 194.—A Spirometer.—(*Boruttau.*)

Volumes of Air Breathed.—The volumes of air which enter and leave the lungs with each inspiration and expiration naturally vary with the extent of the movement, though four volumes at least, may be determined: (1) that of an ordinary inspiration; (2) that of an ordinary expiration; (3) that of a forced inspiration; (4) that of a forced expiration.

The apparatus employed for the determination of these different volumes is the *spirometer*, a modification of the gasometer. The form introduced by Jonathan Hutchinson, of which Fig. 194 is a modification, consists of two metallic cylinders, one containing water, the other containing air, the latter being inserted into the former. The air cylinder is balanced by a weight so accurately that it remains stationary in any position. A tube, penetrating the base of the water cylinder, is continued upward through and above the level of the water. The air-space above is thus placed in free communication with the atmospheric air. A stopcock at the outer end of this tube prevents the escape of the air when this is not desirable. To the free end of the tube a rubber tube provided with a suitable mouthpiece is attached, through which air can be breathed into or out of the air cylinder. With each inspiration the air cylinder descends; with each expiration it ascends. A scale, on the side support, graduated in cubic inches or centimeters, indicates the volume of air inspired or expired.

With an apparatus of this character Hutchinson, from a long series of observations, defined and determined the above-mentioned four volumes as follows:

1. The *tidal* volume, that which flows into and out of the lungs with each inspiration and expiration, which varies from 20 to 30 cubic inches (330 to 500 c.c.).
2. The *complemental* volume, that which flows into the lungs, in addition to the tidal volume, as a result of a *forcible inspiration*, and which amounts to about 110 cubic inches (1800 c.c.).
3. The *reserve* volume, that which flows out of the lungs, in addition to the tidal volume, as a result of a *forcible expiration*, and which amounts to about 100 cubic inches (1650 c.c.).

   After the expulsion of the reserve volume there yet remains in the lungs an unknown volume of air which serves the mechanic function of distending the air-cells and alveolar passages, thus maintaining the conditions essential to the free movement of blood through the capillaries and to the exchanges of gases between the blood and alveolar air. As this volume of air cannot be displaced by volitional effort, but resides permanently in the alveoli and bronchial tubes though constantly undergoing renewal, it was termed—
4. The *residual* volume, the amount of which is difficult of determination, but has been estimated by different observers at 914 c.c., 1562 c.c., 1980 c.c.

The Vital Capacity of the Lungs.—From foregoing statements it is clear that the thorax and lungs are capable of a maximum degree of expansion, at which moment the lungs contain their maximum volume of air. This volume, whatever it may be, represents the entire capacity of the lungs in the physiologic condition, and includes the tidal, the complemental, the reserve, and the residual volumes. Mr. Hutchinson, however, defined the vital or respiratory capacity of the lungs as the amount of air which can be expelled by the most forcible expiration after the most forcible inspiration, this therefore *excludes* the residual volume. The vital capacity was supposed to be an indication of an individual's respiratory power, not only in physiologic but also in pathologic conditions. Though averaging about 230 cubic inches (3770 c.c.) for an individual 5 feet 7 inches in height, the vital capacity varies with a number of conditions, the most important which is stature. It is found that between 5 and 6 feet the capacity increases 8 inches (130 c.c.) for each inch increase in height.

The Total Volume of Air Breathed Daily.—For the solution of certain problems connected with ventilation it is necessary to determine the total volume of air taken into the lungs in the course of 24 hours. This can be determined approximately if the two factors, the average volume of air taken into the lungs at each inspiration, and the average number of respirations per minute be known. If it be accepted that the inspired volume varies from 328 to 492 c.c. and that the respiratory frequency averages 18 per minute, then the total volume breathed would amount to from 8500 to 12,752 liters.

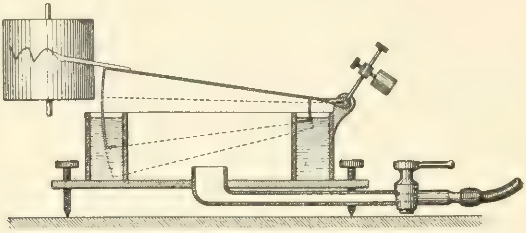


FIG. 195.—GAD'S PNEUMATOGRAPH.

The volume changes of the thorax indicated by the volumes of air entering and leaving the lungs can be not only determined but graphically represented by means of an apparatus similar in principle to the spirometer, devised by Gad and known as the *pneumatograph* or *aëroplethysmograph* (Fig. 195). This consists of a quadrangular box with double walls, the space between which is filled with water. The center of the box is an air chamber. A thin walled mica box sinks into the water. Posteriorly it is attached to and rotates around an axis, which permits of an elevation or depression of the anterior portion. It is also carefully counterpoised. A light lever attached to the mica box records its movements. The interior of the box communicates by a tube with a large reservoir into which the individual breathes, the object being to prevent a too rapid vitiation of the

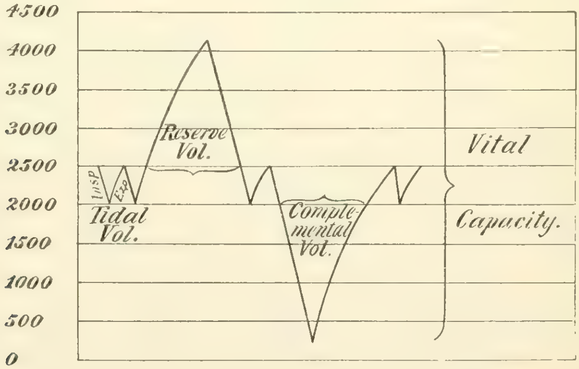


FIG. 196.—DIAGRAM REPRESENTING THE VOLUME CHANGES OF THE THORAX AND LUNGS.—(*Modified from Boruttau.*)

air. Inspiration causes the lever to descend, expiration to ascend. Previous graduation of the apparatus is necessary to determine the volumes breathed. A graphic record of the volume changes is shown in Fig. 196.

Respiratory Sounds.—On applying the ear over the trachea and bronchi there is heard during both inspiration and expiration a well-defined sound, which is loud, harsh, and blowing in character, and which from its situation is known as the *bronchial* sound. It is especially well heard between the scapulæ above the level of the fourth thoracic vertebra. This sound is produced in the larynx, for with its separation from the trachea the sound disappears. The cause of the sound is to be found in the narrowing of the air-passage at the level of the vocal membranes, though the mechanism of its production is uncertain. On applying the ear to almost any portion of the chest-wall, but especially to the infrascapular area, there is heard during both inspiration and expiration a delicate, sighing, rustling sound, which from its supposed seat of origin, the air-vesicles or air-cells, is known as the *vesicular* sound. This sound is supposed to be due to the sudden expansion of the air-cells during inspiration and to the friction of the air in the alveolar passages.

THE CHEMISTRY OF RESPIRATION

The general metabolic process as it takes place in the tissues involves the assimilation of oxygen and the evolution of carbon dioxid. The former is the first, the latter the last, of a series of chemic changes the continuance of which is essential to the maintenance of all life phenomena. A constant supply of oxygen and an equally constant removal of carbon dioxid are necessary conditions for tissue activity. The blood is the medium by which the oxygen is transported from the lungs to the tissues and the carbon dioxid from the tissues to the lungs. The respiratory movements constitute the means by which the oxygen of the air is brought into, and the carbon dioxid expelled from, the lungs into the surrounding air.

The exchanges between the blood and the tissues constitute *internal* respiration, while the exchanges between the blood, the intra-pulmonic and the atmospheric air, the result of the mechanic movements of the thorax, constitute *external* respiration. The transfer of the oxygen by the blood from the interior of the lungs to the tissues, and of the carbon dioxid from the tissues to the interior of the lungs, is the outcome of a series of physical and chemic changes which are related to the exchange of gases between the air in the lungs and the blood, on the one hand, and the exchange of gases between the blood and tissues, on the other hand.

In consequence of the many and complex chemic changes which attend these gaseous exchanges, there arise changes in composition of:

1. The air breathed.
2. The blood, both arterial and venous.
3. The tissue elements and the lymph by which they are surrounded.

The investigation of the nature of these changes, the mechanism of their production, and their quantitative relations constitute the subject-matter of the chemistry of respiration.

CHANGES IN THE COMPOSITION OF THE AIR

Experience teaches that the air during its sojourn in the lungs undergoes such a change in composition that it is rendered unfit for further breathing.

Chemic analysis has shown that this change involves a loss of oxygen, a gain in carbon dioxid, watery vapor, and organic matter. For the correct understanding of the phenomena of respiration it is essential that not only the character but the extent of these changes be known. This necessitates an analysis of both the inspired and expired airs, from a comparison of which certain deductions can be made.

The results which have been obtained are represented in the following table:

	Inspired Air.	
100 vols.	Oxygen	20.80.
	Carbon dioxid	traces.
	Nitrogen	79.20.
	Watery vapor	variable.

	Expired Air.	
100 vols.	Oxygen	16.02.
	Carbon dioxid	4.38.
	Nitrogen	79.60.
	Watery vapor	saturated.
	Organic matter	a trace.

These analyses indicate that under ordinary conditions the air loses oxygen to the extent of 4.78 per cent. and gains carbon dioxid to the extent of 4.38 per cent.; that it gains in nitrogen to the extent of 0.4 per cent. and in watery vapor from its initial amount to the point of saturation, as well as in organic matter. It is to these changes in their totality that those disturbances of physiologic activity are to be attributed which arise when expired air is re-breathed for any length of time without having undergone renovation.

Special forms of apparatus have been devised for the collection and analysis of gases. Their construction as well as the methods of analysis involved are complicated and need not be described in this connection. The presence of the carbon dioxid, however, may be readily shown by breathing through a glass tube into a vessel containing barium or calcium hydrate solution. The turbidity which immediately follows is due to the formation of barium or calcium carbonate, which can be due only to the presence of carbon dioxid. That this turbidity is not due to the carbon dioxid normally present in the air is shown by the fact that the solution remains clear until the passage of the atmospheric air has been maintained for some time. From the percentage loss of oxygen and gain in carbon dioxid, the total oxygen absorbed and carbon dioxid exhaled may be approximately calculated. Thus, if the volume of air breathed daily be accepted at either 8,500 or 12,752 liters, and the percentage loss of oxygen be 4.78, the total oxygen absorbed may be obtained by the rule of simple proportion, *e.g.*:

$100 : 4.78 :: 8{,}500 : x = 406$ liters or 580 grams[1]

Or

$100 : 4.78 :: 12{,}752 : x = 609$ liters or 870 grams.

By the same method the total carbon dioxid exhaled is found to be either 372 liters or 735 grams, or 558 liters or 1103 grams; volumes in both instances which agree very well with volumes obtained by other methods.

From the fact that only 558 liters of carbon dioxid are exhaled as compared with 609 liters of oxygen absorbed, it is evident that not all of the oxygen unites with carbon to form carbon dioxid and that the remainder of the oxygen must unite with some other element. As there is usually an excess of water eliminated over that introduced into the body, it is highly probable that the oxygen combines with free hydrogen to form water. The relative amounts of the oxygen so utilized are not fixed but variable, and depend on the quality and quantity of the foods, exercise, etc. The ratio of the volume of the carbon dioxid exhaled to the volume of oxygen absorbed is known as the *respiratory quotient*, and is usually represented by the symbol $\frac{CO_2}{O^2}$. Thus in the foregoing analysis the respiratory quotient is 0.916.

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[1] 1 liter of oxygen weighs 1.4298 grams; 1 liter of carbon dioxid weighs 1.977 grams.

The gain in nitrogen is a variable factor, ranging from zero to 0.9 per cent. This gain is probably of accidental occurrence, due to absorption from the large intestine, in which decomposition of nitrogen-holding compounds is taking place. It is generally believed that free nitrogen plays no part in any phenomenon of combination or decomposition within the body.

The gain in watery vapor will depend on the amount previously present in the air. This is conditioned by the temperature. With a rise in temperature the percentage of water increases; with a fall, it decreases. By breathing into a vessel containing pumice stone saturated with sulphuric acid, the vapor may be collected. The difference observed between the weight before and after breathing is an indication of the amount by weight of water exhaled during the time of breathing. It has been calculated that the amount of water exhaled daily varies between 300 and 500 grams. Though invisible at ordinary temperatures, it becomes visible at low temperature as soon as it emerges from the respiratory tract. The loss of heat is followed by a condensation of the vapor, which appears at once as a cloudy precipitate.

The gain in organic matter is also variable. The amount present is not sufficient to permit of a thorough chemic analysis, but there are reasons for believing that it belongs to the proteid group of bodies. If it accumulates in the air, especially at high temperatures, it readily undergoes decomposition, with the production of offensive odors. Traces of free ammonia have also been found in the expired air. In addition to these chemic changes, the air experiences physical changes; *e.g.*, a rise in temperature and an increase in volume. The rise in temperature can be shown by breathing through a suitable mouthpiece into a glass tube containing a thermometer. By this means it has been shown that inspired air at 20°C. rises in temperature to 37°C.; at 6.3° to 29.8°C. The increase in the temperature will depend upon that of the air inspired and the time it remains in the lungs. If retained a sufficient length of time it will always become that of the body. As a result of the heat absorption the expired air increases in volume about one-ninth of that of the inspired air. When corrected for temperature and pressure and freed from aqueous vapor, the volume of the expired air is less than that of the inspired air by about one two-hundred and fiftieth.

The Composition of the Alveolar Air.—The foregoing statement of the composition of the expired air, derived in part from the upper air-passages, trachea, and bronchi, does not necessarily represent the composition of the alveolar air. It is very probable that the percentage of carbon dioxid is greater, the percentage of oxygen less, in the latter than in the former. This is made evident by collecting in several portions the expired air as it escapes from the respiratory tract and subjecting it to analysis. The last portion always contains a larger amount of carbon dioxid and a smaller amount of oxygen than the first portion. The determination of the composition of the alveolar air is extremely difficult. It has been estimated to contain from 5 to 6 per cent. of carbon dioxid and from 14 to 18 per cent. of oxygen.

Pulmonary Ventilation.—It is owing largely to this inequality of volumes and consequently of the "partial pressures" of these two gases in the trachea and alveoli that the degree of ventilation necessary for the exchange of gases between lungs and air is maintained. Though the respiratory movements doubtless create currents in the air-passages which carry, on the one hand, a portion of the inspired air directly into the alveoli, and, on the other hand, carry a portion of the alveolar air directly out of the body, other portions find their way into and out of the alveoli in accordance with the laws of diffusion. If the pressure of the oxygen in the trachea is 158 mm. Hg. and in the alveoli approximately 122 mm. Hg., diffusion downward will take place. Equilibrium, however, is never established, as the oxygen is continually disappearing by passing into the blood. On the contrary, if the carbon dioxid pressure in the alveoli is approximately 28 to 40 mm. Hg., and in the trachea 0.3 mm. Hg., diffusion will take place upward. Equilibrium will never be established, however, as the carbon dioxid is constantly coming out of the blood. Pulmonary ventilation may also be aided by those alternate changes in volume of the heart, great vessels, and lungs occurring as the result of the heart-beat and producing the so-called cardio-pneumatic movements.

CHANGES IN THE COMPOSITION OF THE BLOOD

The blood which flows through the pulmonic artery into the lungs is dark bluish-red, while that which flows from the lungs into the pulmonic veins is scarlet red, in color. The blood is changed, while flowing through the lung capillaries, from the venous to the arterial condition. As the air in the lungs gains carbon dioxid, and loses oxygen it is fair to assume that what the air gains the blood loses, and what the air loses the blood gains. In other words, the blood, while passing through the lungs, is changed from venous to arterial by the loss of carbon dioxid and the gain of oxygen. The change in color of venous blood from dark bluish, to scarlet red is strikingly shown by shaking it in a test-tube with oxygen or atmospheric air.

The blood which flows through the arteries into the tissues is scarlet red, while that which flows from the tissues into the veins is bluish-red in color. The blood while flowing through the tissue capillaries is changed from the arterial to the venous condition. Since arterial blood when deprived of oxygen becomes bluish-red, the indication is that the change in color is associated with, if not entirely due to, the escape of oxygen into the tissues. The constant elimination of carbon dioxid from the blood into the lungs indicates that the carbon dioxid is as constantly passing from the tissues across the capillary walls into the blood.

These considerations are confirmed by the results of analyses which have been made of both arterial and venous blood. The presence of gas in the blood is demonstrated by subjecting it under appropriate conditions to the vacuum of the mercurial air-pump, into which it at once escapes. From 100 volumes, an average of 60 volumes of gas at standard pressure, 760 mm. Hg. and temperature 0°C., can thus be obtained.

Gases of the Blood.—An analysis of the volumes of gas removed from both arterial and venous blood shows that each consists of oxygen, carbon dioxid, and nitrogen, though in different amounts. Average compositions of the gases extracted from dog's blood obtained from the carotid artery and right ventricle respectively are given in the following table:

Arterial blood 100 vols.	Oxygen	20 vols.	Venous blood 100 vols.	Oxygen	12 vols.
	Carbon dioxid	40 vols.		Carbon dioxid	45 vols.
	Nitrogen	1–2 vols.		Nitrogen	1–2 vols.

The changes produced in the blood by respiration, both external and internal, become apparent from a comparison of these analyses. The arterial blood while passing through the capillaries of the tissues loses eight volumes per cent. of oxygen and gains five volumes per cent. of carbon dioxid. The venous blood while passing through the capillaries of the lungs gains oxygen and loses carbon dioxid in corresponding amounts. These amounts will vary somewhat in the analyses of the blood of different animals and under different physiologic conditions. The volume of nitrogen is not appreciably changed.

The Relation of the Gases in the Blood.—The mechanism by which the gases become associated with the blood at the moment of their entrance into it, and again become dissociated just prior to their exit from it, as well as their relation to the blood while in transit, will be more readily understood after reference to a few elementary facts relative to the absorption of gases by liquids in general and the conditions of temperature and pressure by which it is influenced.

It is well known that liquids will absorb or dissolve at any constant pressure unequal volumes of different gases in accordance with their solubilities and with variations in temperature. Water, for example, will absorb, in accordance with the foregoing conditions, oxygen, carbon dioxid, and nitrogen, as well as many other gases. The volume of any gas thus absorbed is known as the *coefficient of absorption*, and may be defined as the number of cubic centimeters of the gas which one cubic centimeter of water will absorb when the gas, in contact with the water, stands under a pressure of one atmosphere or 760 mm. of mercury and at a temperature of 0°C. The volume absorbed, however, varies inversely as the temperature. Thus at 0°C. the volume of oxygen absorbed by one volume of water is 0.0489 c.c.; of carbon dioxid 1.713 c.c.; of nitrogen 0.0234 c.c. With a rise of temperature, the pressure remaining constant, the absorptive power of water for each of these gases diminishes. Thus at 15°C., the volumes of oxygen, carbon dioxid and nitrogen absorbed are 0.0310 c.c., 1.0025 c.c. and 0.0168 c.c. respectively. Though the volume of the gas absorbed diminishes as the temperature rises, it is independent of pressure, for no matter to what extent the pressure may vary the *volume* absorbed is always the same. (Law of Henry.)

If the *weight* of the gas absorbed be considered rather than the volume (that is the product of the volume and the density or the number of molecules in the volume), then the temperature remaining constant, the weight of the volume absorbed increases and decreases proportionately as the pressure rises and falls. Thus at a pressure of 760 mm. of mercury and at a temperature of 0°C., the volume of oxygen absorbed by one volume of water is 0.0489 c.c.; at 1520 mm. of mercury, the *same volume* is absorbed but its *weight* is doubled. If the pressure falls below 760 mm. of mercury the *same volume* is absorbed but its weight is diminished. (Law of Dalton.) Because of the foregoing facts, it is necessary in all gaseous determinations to reduce for purposes of comparison the obtained volumes to standard temperature (0°C.) and pressure (760 mm. of mercury).

When the liquid is once saturated with a gas at a constant pressure and temperature, there is coincidently with the entrance of the gas into the liquid, an equivalent exit of the gas from it, though the volume retained in the liquid remains constant. The reason for this fact is, that under the conditions, the volume of the gas dissolved by the liquid though *small in amount* exerts a pressure in the opposite direction equivalent to the pressure acting upon the liquid. If one cubic centimeter of water absorbs 0.0489 c.c. of oxygen at 760 mm. and 0°C., this volume will exert a pressure opposite in direction of 760 mm. of mercury. For this reason the entrance and exit of the gas are equal and opposite.

If water be exposed to atmospheric air consisting of oxygen, carbon dioxid, and nitrogen in the ordinary proportions, at any given temperature and pressure, the water will absorb unequal volumes of each of the three gases. The pressure under which each gas is absorbed is a part only, however, of the total atmospheric pressure at the time. The pressure exerted by any one of these gases is known as its "partial pressure," and depends on the percentage volume of the gas present. If atmospheric air contains at standard pressure and temperature 79.15 volumes per cent. of nitrogen, its partial pressure will be $\frac{79.15}{100}$ of 760, or 601.54 mm. Hg.; if the air contains 0.04 volume per cent. of carbon dioxid and 20.85 volumes per cent. of oxygen, the partial pressure of each will be 0.30 mm. Hg. and 158.46 mm. Hg. respectively. The absorption of each gas is independent of all the rest, and is the same for nitrogen, for example, as if it alone were present at a pressure of 601.54 mm. Hg.

Again, if water holding in solution a certain volume of a gas—carbon dioxid, for example—be exposed to an atmosphere containing but 0.04 volume per cent. of carbon dioxid, and having therefore a pressure of but 0.3 mm. Hg., the gas will at once begin to leave the water, and continue to do so until the pressure of the carbon dioxid in the atmosphere balances the pressure of the gas in the water, at which moment the escape of the gas ceases. The pressure of a gas in a liquid is equal to that pressure in millimeters of mercury of the same gas in the atmosphere which is required to keep it in solution. What is true for the carbon dioxid is true for any other gas that may be in solution. If a liquid has a greater density than water, as from the presence of inorganic salts, the absorptive power under standard conditions of temperature and pressure becomes less. It is for this reason that blood-plasma contains less oxygen, nitrogen, and carbon dioxid than water.

It will be recalled that the blood yields up its gases when subjected to the vacuum of the mercurial pump; that is, to a diminution or complete removal of the atmospheric pressure. From this it might be inferred that the gases are merely held in solution by pressure, and at once escape the moment they are exposed to a space in which there is a very slight or a total absence of pressure. In other words, that the absorption of gases by the blood and their escape from it follow the law of pressure as stated in foregoing paragraphs. It is therefore necessary to test this supposed condition of the gases in the blood by subjecting the latter to gradually diminishing pressures, with a view of determining in how far the discharge of the gases follows the law of falling pressures. For convenience the conditions of each gas will be considered separately.

Oxygen.—If blood is subjected to a succession of pressures progressively less than the standard, it is found that though oxygen is evolved, its evolution is not in accordance with the law of partial pressures; that is, in proportion to the diminution of pressure. Within wide limits—*e.g.*, from 760 to 332 mm. atmospheric pressure, to which correspond oxygen pressures of 159 and 70 mm. respectively—there is but a slight increase in the amount of oxygen evolved; and it is not until the pressure of the oxygen falls below the latter, *i.e.*, 70 mm. that it begins to be liberated in large amounts. From this on, the oxygen continues to be liberated with decreasing pressures, until the zero point is reached, when all gaseous discharge ceases. Coincidently the blood changes in color from a bright red to a deep bluish-red. It is evident from the results of this procedure that the condition of the oxygen in the blood is but to a slight extent one of physical absorption. The indications are that the union is of the nature of a chemic combination.

If the red corpuscles are removed from the blood and the plasma alone treated in the manner above described, it will be found that the oxygen liberated now follows the law of partial pressure. The amount so liberated, however, is small, scarcely amounting to more than 0.36 c.c. per 100 c.c. of blood. The agent therefore which holds the oxygen in combination is the red corpuscle, or more exactly, the hemoglobin, which constitutes about 32 per cent. of its volume. This is proved by the fact that a solution of gas-free hemoglobin of a strength equivalent to that of the blood (14 per cent.), exposed to oxygen under a gradually increasing pressure from zero up to 50 to 70 mm. pressure, will absorb large quantities of oxygen; beyond this point the amount absorbed is again small in comparison. At 70 mm. pressure the hemoglobin is almost saturated. Coincidently with this absorption the hemoglobin changes in color from bluish-red to scarlet-red and changes from hemoglobin to oxyhemoglobin. The reverse method, that of subjecting oxyhemoglobin to gradually diminishing pressures, yields opposite results, that is, the oxygen becomes dissociated and the force by which this is accomplished is known as the force of dissociation. As one gram of hemoglobin combines with 1.34 c.c. of oxygen, and as the percentage of hemoglobin is 13.50 to 14, it is evident that there is sufficient hemoglobin to combine with practically all the oxygen usually present in the blood. Thus the hemoglobin in 100 c.c. of blood would hold in combination 18.76 c.c. of oxygen. This, together with the one c.c. held in solution in plasma, would equal the volume obtained in the vacuum of the air-pump.

The union of the oxygen with the hemoglobin is therefore largely chemic in character, dependent however on pressure. About one per cent. is physically absorbed by or dissolved in the plasma; the remainder is chemically combined with the hemoglobin.

The association or combination of oxygen is favored by a pressure of at least 30 to 50 mm. Hg. and upward; the dissociation, by diminution of pressure. In the conversion of hemoglobin into oxyhemoglobin two antagonistic forces are at work, heat and chemic affinity. The former tends to prevent, the latter to favor, the union. Chemic affinity increases with the influence of mass, that is, in proportion to the number of atoms in a unit of volume, with the density, and with the partial pressure of the oxygen. Diminution of pressure reduces the mass influence and permits the heat to bring about dissociation (Bunge). The following table by Hüfner shows the relative proportion of hemoglobin and oxyhemoglobin in blood containing 14 per cent. hemoglobin and exposed to air at gradually diminishing pressures:

Atmospheric Pressure in mm. Hg.	Partial Pressure of Oxygen in mm. Hg.	Hemoglobin Percentage.	Oxyhemoglobin Percentage.
760	159.3	1.49	98.51
524.8	110	2.14	97.86
357.8	75	3.11	96.89
238.5	50	4.60	95.40
119.3	25	8.79	91.21
47.7	10	19.36	80.64
23.8	5	32.51	67.49
0.0	0.0	100.00	0.00

Carbon Dioxid.—The blood yields up its contained carbon dioxid to the vacuum of the gas-pump as completely as it does its oxygen. The same is not the case, however, if the red corpuscles are first removed and the experiment made with either plasma or serum. Even at zero pressure the fluid contains carbon dioxid, as shown by its liberation on the addition of some weak acid, as tartaric or phosphoric, an indication that it exists in a state of firm combination. The same result follows the addition of the red blood-corpuscles, which act in a manner similar to the acids just mentioned. This property of the corpuscles has been attributed to hemoglobin, and especially when in the state of oxyhemoglobin. It is for this reason that blood yields all its carbon dioxid to the vacuum of the gas-pump.

The limit of pressure at which the plasma ceases to absorb carbon dioxid physically and begins to combine it chemically is not very clearly defined. It has been estimated that of the entire amount, 38 to 45 volumes, only about 2.5 volumes are so absorbed, the remainder being in a condition of both loose and stable combination.

An analysis of the serum, and presumably of the plasma, shows the presence of sodium salts, with which the carbon dioxid could enter into combination, viz.: sodium carbonate and dibasic sodium phosphate. The sodium is thus partly divided between carbonic acid and phosphoric acid. The amount of the sodium which falls to carbon dioxid will depend on the mass influence of the latter; that is, its partial pressure.

At its origin in the tissues the carbon dioxid acquires a considerable tension, and its mass influence is correspondingly large. On entering the blood it combines with sodium carbonate, with the formation of sodium bicarbonate, as shown in the following equation:

$$Na_2CO_3 + CO_2 + H_2O = 2NaHCO_3.$$

At the same time, having a greater mass influence than the phosphoric acid, it will withdraw from the dibasic sodium phosphate one-half of its sodium, with the formation of sodium bicarbonate and monobasic sodium phosphate, as shown in the following equation:

$$Na_2HPO_4 + CO_2 + H_2O = NaHCO_3 + NaH_2PO_4.$$

In addition to the amount of CO_2 physically absorbed by the plasma and chemically combined with sodium, a third portion is more or less loosely combined with the protein constituent, globin, of the red corpuscle. As this is the case the corpuscles must be regarded as carriers of CO_2 from the tissues to the lungs as well as carriers of oxygen. It has also been suggested that the presence of the CO_2 in the corpuscle, assists in the dissociation of the oxygen as the blood passes through the capillaries. With the diffusion of the carbon dioxid from the blood into the alveoli its tension in the venous blood falls, its mass influence diminishes, while that of the phosphoric acid relatively increases. As a result, the sodium is withdrawn from the sodium bicarbonate, an additional liberation of carbon dioxid takes place and dibasic sodium phosphate is re-formed. The association or combination of the carbon dioxid with the basic salts depends on its partial pressure; dissociation in the lungs, on a diminution of pressure.

Nitrogen.—This gas exists in both arterial and venous blood in a state of solution. There is no evidence that it enters into combination with any other element.

Tension of the Gases in the Blood.—It will be recalled that a liquid holding in solution one or more gases will on exposure to an atmosphere composed of the same gases either give up or absorb volumes varying in amount and in accordance with their partial pressures until equilibrium is established. If the pressure of any one gas in the atmosphere is greater than the pressure of the same gas in the liquid, it is absorbed; if the pressure is less the gas is discharged. Knowing the pressure of the gases in percentages of an atmosphere, at the beginning and the end of an experiment, the original tension or pressure of the gases in the liquid can be easily calculated. On this principle various forms of apparatus known as *aërotonometers* have been devised by which the tension of the gases in the blood can be determined.

These appliances consist essentially of a glass tube containing oxygen, carbon dioxid, and nitrogen in known amounts and tensions. The blood from an animal is then allowed to flow directly from an artery or vein into the tube. As it flows down its sides in a thin layer it presents a large surface to the action of the contained gases. In the aërotonometer of Fredericq the blood, made non-coagulable by the injection of peptone, is returned from the opposite extremity of the tube to the animal. This enables the experiment to be continued for an hour or more. A knowledge of the tensions of the blood gases is of interest, as it affords a clue to the mechanism by which the interchange takes place between the lungs and the blood, on the one hand, and the blood and tissues, on the other. The results, however, of different observers are not sufficiently in accord to permit of positive deductions.

In the well-known experiments of Strassburger, the tension of the oxygen in the arterial blood of the dog was found to be 29.64 mm. Hg., or 3.9 per cent, of an atmosphere, and in the venous blood 22.04 mm. Hg., or 2.9 per cent. The tension of the carbon dioxid in the venous blood was found to be 41.14 mm. Hg., or 5.4 per cent. of an atmosphere, and in the arterial blood 21.8 mm. Hg., or 2.8 per cent. Very different results have been obtained by Fredericq with the aërotonometer devised by him and by the employment of a method different from that of Strassburger. Thus he states that the oxygen tension in the pulmonic alveoli is 136 mm. Hg., or 18 per cent. of an atmosphere while in the arterial blood it is 106 mm. Hg., or 14 per cent.; while the carbon-dioxid tension in the tissues varies from 45 to 68 mm. Hg., or from 6 to 9 per cent. of an atmosphere; while in the venous blood it varies from 30 to 41 mm. Hg., or from 3.8 to 5.4 per cent. and in the pulmonic alveoli it is about 21 mm. or 2.8 per cent.

CHANGES IN THE COMPOSITION OF THE TISSUES AND LYMPH

From previous statements the inferences can be drawn that the oxygen leaves the blood as the latter flows through the capillaries; that it passes through the capillary wall into the surrounding lymph and so to the tissue-cells; that it oxidizes food materials in the tissue-cells whereby the potential energy of the former is liberated as kinetic energy; that the carbon dioxid so evolved passes into the lymph and through the wall of the capillary into the blood.

While this is doubtless the case, the presence of free oxygen in the tissues cannot be demonstrated by the usual methods of gas analysis. Only in the saliva and in the blood of the placental umbilical vein can it be shown that oxygen has directly passed through the capillary wall. For this reason it has been claimed by a few investigators that oxygen does not leave the blood, but that the field of its activity as an oxidizing agent is limited to the blood-current, where it meets with and oxidizes easily reducible substances entering from the tissues. On this view the potential energy of the food would be liberated by mere decomposition or cleavage in consequence of cell activity.

Nevertheless many facts from the fields of comparative physiology and physiologic chemistry combine to support the view that oxygen is absolutely necessary to the maintenance of the life of all tissue cells. Though they will continue to manifest their characteristic activities—*e.g.*, contraction on the part of a muscle, secretion by a gland, the conduction of a nerve impulse by the nerve, etc.—for a variable length of time after oxygen is prevented from gaining access to them, nevertheless they will in due time die.

The necessity for oxygen on the part of the tissues and the avidity with which they absorb it, is shown by their power of reducing pigments such as alizarine blue. If this pigment be injected into the blood-vessels of an animal and the animal killed in about ten minutes, it will be found that while the blood exhibits a deep blue color the tissues present their usual colors. But after exposure to the air or to free oxygen the latter also acquire the characteristic blue color. The explanation offered for this fact is that the tissues in their need for oxygen absolutely extract it from the pigment, reducing it to a colorless compound, which, however, on exposure recombines with oxygen and regains the original color.

Though free oxygen cannot be shown to be present in the tissues, there are many reasons for believing that it is continually passing into them by way of the lymph-stream. Its rapid disappearance would indicate that it is immediately utilized for the production of carbon dioxid (which is improbable on other grounds), or that the tissues possess a capacity for oxygen storage, of placing it in reserve under some combination or other, by which it can be securely retained until required for oxidation purposes. This is rendered probable from the fact that the carbon dioxid evolved at any given moment is not necessarily dependent on the oxygen just absorbed, for if oxygen be withheld from a nutritive fluid which is being artificially circulated through a recently isolated organ, carbon dioxid will continue to be discharged for some time. A muscle, or even a living animal—*e.g.*, a frog—placed in an atmosphere of pure nitrogen will remain active and evolve CO_2 even for several hours.

Naturally the absorption of oxygen and the discharge of carbon dioxid and the changes of composition which are incident to nutrition will be most marked in those tissues characterized by the greatest degree of physiologic activity. Muscle-tissue exhibits these changes to a greater degree than bone. Tissues with intermediate degrees of activity should exhibit corresponding degrees of respiratory change. Experiment confirms this view. Thus, 100 grams each of muscle, spleen, and broken bone from a recently living animal exposed to the air for twenty-four hours absorbed respectively 50.8 c.c., 27.3 c.c., and 17.2 c.c. of oxygen, while each discharged during the same period 56.8 c.c., 15.4 c.c., and 8.1 c.c. of carbon dioxid respectively.

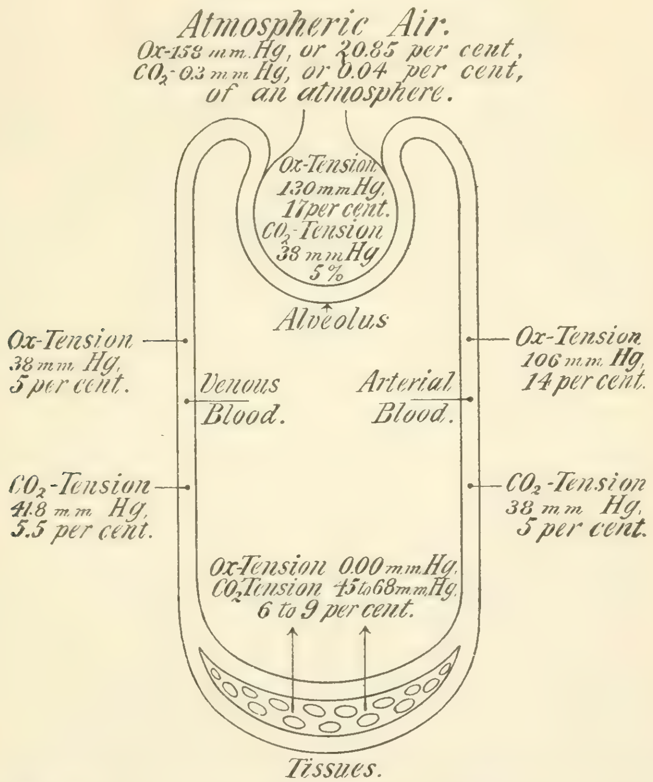
Atmospheric Air.
Ox-158 mm. Hg, or 20.85 per cent,
CO_2-0.3 mm. Hg, or 0.04 per cent,
of an atmosphere.
Ox-Tension 130 mm Hg. 17 per cent.
CO_2-Tension 38 mm Hg 5%
Alveolus
Ox-Tension 38 mm. Hg, 5 per cent.
Venous Blood.
Arterial Blood.
Ox-Tension 106 mm. Hg, 14 per cent.
CO_2-Tension 41.8 mm. Hg, 5.5 per cent.
CO_2-Tension 38 mm. Hg, 5 per cent.
Ox-Tension 0.00 mm. Hg.
CO_2 Tension 45 to 68 mm. Hg.
6 to 9 per cent.
Tissues.

FIG. 197.—DIAGRAM SHOWING THE RELATIVE TENSION OF OXYGEN AND CARBON DIOXID IN THE LUNGS, IN THE BLOOD, AND IN THE TISSUES.

In another series of experiments by a different observer 100 grams of muscle absorbed in three hours 23 c.c. of oxygen, and 100 grams of bone 5 c.c. of oxygen. Both tissues discharged carbon dioxid in amounts proportional to the oxygen absorbed. The same respiratory changes may be more satisfactorily demonstrated by passing blood through the tissues of isolated organs and the tissues of recently living animals. The analysis of the blood before and after perfusion shows a loss of oxygen and a gain in carbon dioxid.

Tension of the Gases in the Tissues.—As the presence of free oxygen cannot be demonstrated, its tension there must be regarded as *nil*. The tension of the carbon dioxid is quite high, though difficult of exact determination. It has been estimated at from 45 to 68 mm. Hg., or from 6 to 9 per cent. of an atmosphere.

The variations of tension or pressure of these two gases in the lungs, in different parts of the vascular apparatus, and in the tissues, and their relations to each other, are shown in Fig. 197, expressed in mm. Hg. and percentages of an atmosphere.

The Mechanism of the Gaseous Exchange.—In these pressure differences sufficient cause is found for the exchange of the gases. The oxygen pressure in the alveoli being in excess of that in the blood, the gas passes through the thin alveolo-capillary wall into the plasma. As the oxygen pressure in the plasma rises and approximates that in the alveoli, a portion of the oxygen combines with the hemoglobin until the latter is almost saturated. The corpuscle is then carried through the arterial system surrounded by oxygen under a definite pressure which is sufficient to keep the absorbed oxygen in union with the hemoglobin. On passing into the systemic capillaries, the blood enters a region in which the oxygen tension in the surrounding tissues is *nil.* At once the oxygen dissolved in the plasma passes through the capillary wall into the surrounding tissue-spaces. The pressure removed from the corpuscle, a dissociation of the oxygen and of the hemoglobin takes place, after which the dissociated oxygen also passes through the capillary wall into the surrounding lymph and so to the tissue cells where it is stored and utilized. On passing into the venous system the dissociation of the oxygen and the hemoglobin is checked by the rise of oxygen pressure in the plasma. On reaching the lungs the oxygen again passes into the blood until the former condition is regained.

The sojourn of the blood in the capillaries being short, the oxyhemoglobin can part with but a portion of its oxygen, sufficient, however, to satisfy the needs of the tissues.

The carbon dioxid pressure in the tissues being in excess of that in the blood, it passes through the capillary wall into the blood, where it exists in the free and combined states. On passing into the pulmonic capillaries the blood enters a region in which the carbon dioxid in the alveoli is less than in the blood. At once a diffusion and dissociation of the carbon dioxid takes place through the alveolo-capillary wall until equilibrium is established. This, however, is of very short duration, for the carbon dioxid so eliminated is rapidly removed from the lungs by the respiratory movements.

While diffusion, in response to physical and chemic conditions, thus plays a large part in, and is sufficient to account for, the exchanges of gases, it is possible that the alveolar or respiratory epithelium may also play an essential rôle. It is believed by some investigators that it is active in both the absorption of oxygen and the excretion of carbon dioxid. This view has been suggested as a means of interpreting the results of the experiments of more recent investigators, made with a view of determining the tension of the blood gases. It was found by Bohr that the tension of the oxygen in arterial blood was often as high as 101 to 144 mm. Hg., and in many instances higher than the tension of the oxygen in the trachea, while the carbon dioxid tension in the trachea was higher than in the blood. Haldane and Smith by a different method found an oxygen tension in the arterial blood of 200 mm. Hg. If these results should prove to be correct, though they are at present subject to considerable criticism and not generally accepted, some other force than diffusion would have to be found to explain the facts. It would then remain to be determined in how far the alveolar epithelium could be regarded as an active agent in both absorption and excretion in opposition to pressure.

THE TOTAL RESPIRATORY EXCHANGE

The total quantities of oxygen absorbed and carbon dioxid discharged by a human being in twenty-four hours are measures of the intensity of the respiratory process, and an indication of the extent and character of the chemic changes attending all life phenomena. Their determination and their relation to each other are matters of interest and importance. The quantities which have been obtained by different observers are the outcome of calculations based on certain groups of data and of experiments made with special forms of apparatus.

Thus from the total air breathed daily, estimated from the amounts obtained during a longer or shorter period by experiments with spirometric apparatus, and from the percentage loss of oxygen and gain of carbon dioxid shown by an analysis of the respired air, it can be calculated at least approximately what the total amounts of oxygen absorbed and carbon dioxid exhaled must be. If it be assumed that the minimum daily volume of air breathed is 8500 liters and the maximum volume 12,752 liters, and the percentage loss of oxygen is 4.78, then the total volume of oxygen absorbed is 406 liters (580 grams) or 609 liters (870 grams). By the same method the total carbon dioxid exhaled daily is found to be either 372 liters (735 grams) or 558 liters (1103 grams). The direct experiments which have been made with specially devised forms of apparatus, both on human beings and animals, have yielded similar results. With those forms which are adapted for both human beings and animals—Scharling's, Pettenkofer and Voit's—it is only possible, however, to determine the amount of carbon dioxid and water exhaled and from them to calculate the amount of oxygen absorbed. This is done by deducting the loss in weight by the man or animal during the experiment from the combined weights of the carbon dioxid and water discharged. The difference represents the oxygen absorbed.

The Pettenkofer-Voit apparatus consists essentially of a chamber large enough to admit a man and capable of being made air-tight with the exception of an inlet for air for breathing purposes. The respired air is drawn through a tube and measured by a large meter turned by a water or gas motor. By means of a side tube a fractional quantity of the main column of air is diverted to an absorption apparatus by a small pump. This air first passes into a vessel containing H_2SO_4, by which the water is collected; then into long tubes containing barium hydroxid, by which the carbon dioxid is absorbed; thence into a small meter, by which its amount is registered. From the amount of water and carbon dioxid thus obtained the amounts of both in the total air breathed are calculated. The water and carbon dioxid previously present in the air are simultaneously determined by a corresponding absorption apparatus and deducted from the amounts obtained from the respired air. As the apparatus is traversed constantly by a column of air of normal composition and the waste products removed as rapidly as discharged, the experiment can be continued for periods varying from six to twenty-four hours without detriment to the subject of the experiment.

With those forms adapted only for animals—Regnault's and Reiset's, or Jolyet and Regnard's—it is possible to determine simultaneously the absorption of oxygen and the discharge of carbon dioxid. As the apparatus employed is completely closed, the carbon dioxid must be removed as soon as discharged and the oxygen renewed as soon as absorbed. The former is accomplished by the aspiratory action of moving bulbs containing an alkali, the latter by a steadily acting pressure on a reservoir of oxygen. This apparatus consists essentially of a glass bell-jar in which the animal is placed. This is brought into connection by tubes, on the one hand, with the oxygen reservoir, and, on the other hand, with the aspiratory bulbs, kept in motion by some form of motor. The construction of each of these forms of apparatus is so complex, the conduct of an experiment and the final determination of the results so complicated, that a detailed description would be out of place in a work of this character.

Of the results obtained by these and other methods a few are given in the following table:

Oxygen Absorbed.	Observer.	Carbon Dioxid Discharged.
746 grams.	Vierordt.	876 grams.
700 grams.	Pettenkofer and Voit.	800 grams.
663 grams.	Speck.	770 grams.

The amounts of oxygen absorbed in Pettenkofer and Voit's experiments varied from 594 to 1072 grams; of carbon dioxid exhaled, from 686 to 1285 grams.

In all these results it is evident on examination that the volume of oxygen absorbed is always greater than the volume of carbon dioxid exhaled, or, what amounts to the same thing, the weight of the oxygen absorbed is always greater than the weight of the oxygen entering into the formation of the carbon dioxid exhaled. The reason for this difference between the amounts of oxygen in the inspired air and in the carbon dioxid exhaled is found in the fact, that on a mixed diet—one containing fat—a portion of the oxygen is utilized in the oxidation of the surplus hydrogen of the fat with the formation of water. Under such a diet the respiratory quotient is always less than unity, usually 0.907. On a purely carbohydrate diet—one in which there is no surplus hydrogen—all the oxygen will combine with carbon and be returned as carbon dioxid, and hence the respiratory quotient will be unity. The respiratory quotient therefore indicates the extent to which the oxygen absorbed is utilized in oxidizing carbon, on the one hand, and hydrogen, on the other.

Since the total oxygen absorbed and carbon dioxid discharged will vary considerably with the size of the animal, it is customary, for purposes of comparison, to reduce all total results to the unit of body-weight (one kilogram) and to the unit of time (one hour).

Respiratory Activity.—The activity or the intensity of the respiratory process may be measured either by the oxygen absorbed or by the carbon dioxid discharged. But as the carbon dioxid is more easily estimated than the oxygen, the former is usually taken as the index of the activity, though there are reasons for believing that it would be more accurately indicated or represented by the oxygen.

Whatever factor may be accepted as the measure, it is certain that the respiratory activity varies in different tissues in accordance with their functional activities, being least in bones and greatest in muscles. This is shown by the relative amounts of oxygen absorbed and carbon dioxid discharged by equal amounts of each of these and other living tissues in twenty-four hours, as given in the following table:

QUANTITY OF O_2 AND CO_2 ABSORBED AND EXHALED DURING TWENTY-FOUR HOURS, IN CUBIC CENTIMETERS

By 100 Grams of:	Oxygen Absorbed.	Carbon Dioxid Exhaled.
Muscle	50.8 c.c.	56.8 c.c.
Brain	45.8 c.c.	42.8 c.c.
Kidneys	37.0 c.c.	15.6 c.c.
Spleen	27.3 c.c.	15.4 c.c.
Testicles	18.3 c.c.	27.5 c.c.
Pounded bones	17.2 c.c.	8.1 c.c.

The total respiratory change therefore of the body as a whole is the resultant of the respiratory changes of its individual organs and tissues, and is conditioned by all influences which retard or hasten their activity. Among these influences the more important are the following:

Muscle Activity.—As the muscles constitute a large part of the body, about 40 per cent., and as muscle-tissue absorbs and discharges relatively large quantities of oxygen and carbon dioxid, it is readily apparent that an increase in their activity would be followed or attended by an increase in the respiratory exchange. In passing from a condition of body repose to one of marked activity there ought to be an increase in the amount of oxygen absorbed and CO_2 discharged. Pettenkofer and Voit found that a man in repose who absorbed daily 807.8 grams of oxygen and discharged 930 grams CO_2, absorbed during work 1006 grams of oxygen and discharged 1137 grams of CO_2. Edward Smith, who estimated only the CO_2, found that a man in repose who discharged carbon dioxid at the rate of 161.6 c.c. per minute increased the amount while walking at the rate of two and three miles an hour to 569 c.c. and 851 c.c. respectively. Similar results have been obtained by other investigators.

Digestive Activity.—The activity of the alimentary canal, involving contraction of its muscle coat through its entire length as well as secretion of its related glands called forth by the ingestion of food, materially influences the absorption of oxygen and discharge of carbon dioxid, independent of the increase due to the oxidation of food materials after absorption. It was found that in a fasting man a dose of sodium sulphate increased the absorption of oxygen as much as 17 per cent. and the discharge of CO_2 24 per cent. (Löwy). It is difficult to determine how much of the increase after a meal is therefore due to food oxidation and how much to functional activity of the canal itself. The consumption of nitrogenized meals, however, has a greater effect than non-nitrogenized meals.

Temperature.—A rise in temperature of the surrounding air has as an effect diminution in the amounts of oxygen consumed and carbon dioxid discharged. A fall in temperature has the opposite effect. Thus a cat at a temperature of 3.2°C. consumed during a period of six hours 21.39 grams of oxygen and discharged 22 grams of carbon dioxid, while at a temperature of 29.6°C. the corresponding amounts for the same period of time were for oxygen 13.9 grams and for carbon dioxid 13.12 grams. Lavoisier and Sequin, having reference only to the oxygen, found that a man at a temperature of 15°C. consumed 38.31 grams of oxygen, while at a temperature of 32.8°C. the corresponding amount was but 35 grams. Similar results have been obtained by other observers with different animals. The explanation of these facts is to be found in the increased activity of all physiologic mechanisms coincident with a fall, and in the decreased activity, coincident with a rise in temperature. The lower temperatures act as a stimulus to the peripheral terminations of the nerve system, bringing about reflexly increased activity of the body at large. The muscles especially are not only reflexly but volitionally excited to greater activity. This leads naturally to an increase in the consumption of oxygen and in the production of carbon dioxid and in the evolution of heat.

In cold-blooded animals the respiratory exchange is influenced in a manner the reverse of that observed in warm-blooded animals. With a rise of external temperature and a corresponding rise of body-temperature the discharge of carbon dioxid steadily increases. Thus a frog in an atmosphere at 0°C. with a body-temperature of 1°C. discharged per kilogram per hour 4.31 c.c. of carbon dioxid; in an atmosphere of 35°C. with a body-temperature of 34°C. there was discharged 325 c.c. per kilo per hour. Intermediate temperatures were attended by corresponding increases in the amounts of CO_2 discharged. The reason for this difference in the two classes of animals is probably to be found in the cold-blooded animals, in the want, of a self-adjusting heat-regulating mechanism.

Age.—In early youth, as a result partly of the more pronounced activity of the nutritive energies and partly of a cutaneous surface relatively greater, as compared with the mass of the body, than in adult life, the absorption of oxygen and the discharge of carbon dioxid are greater both absolutely and relatively. Thus, in a boy of nine and a half years with a weight of 22 kilograms it was found that in twenty-four hours there was a discharge of carbon dioxid amounting to 488 grams, or 0.92 gram per kilo per hour, and in man with a weight of 65.5 kilograms there was a discharge of 804.72 grams, or 0.51 gram per kilo per hour.

THE NERVE MECHANISM OF RESPIRATION

The nerve mechanism by which the respiratory muscles are excited to and coördinated in activity is extremely complex and involves the action of both afferent and efferent nerves and their related nerve-centers in the central nerve system. For the free introduction of air into the lungs it is essential that the nasal and laryngeal passages and the cavity of the thorax be simultaneously enlarged. The muscles by which these results are accomplished have already been mentioned and described. Their simultaneous and coördinate contraction implies the coördinate activity of nerve-centers and their related motor nerves; thus the action of the nasal and laryngeal muscles (the dilatator naris and the posterior crico-arytenoid) involves the activity of the facial and inferior laryngeal nerves respectively, the centers of origin of which lie in the gray matter beneath the floor of the fourth ventricle; the diaphragm and intercostal muscles involve respectively the activity of the phrenic and intercostal nerves, the centers of origin of which lie in the anterior horn of the gray matter of the spinal cord at a level, for the phrenic, of the fourth, fifth, and sixth cervical nerves, and for the intercostals at the level of the upper thoracic nerves. Division of any one of these nerves is followed by paralysis of its related muscle.

Inspiratory Center.—The coördinate contraction of the inspiratory muscles implies a practically simultaneous discharge of nerve impulses from each of the foregoing nerve-centers, accurately graduated in intensity in accordance with inspiratory needs. This has been supposed to necessitate the existence in the central nerve system of a single group of nerve-cells from which nerve impulses are rhythmically discharged and conducted to the previously mentioned nerve-centers in the medulla oblongata and spinal cord, by which they are in turn excited to activity. To this group of cells the term "inspiratory center" has been given.

For the free exit of air from the lungs it is essential not only that the air-passages be open, but that the air in the lungs be compressed until its pressure rises above that of the atmosphere. This is accomplished by the recoil of the elastic tissue of the lungs and thorax, the return of the displaced abdominal organs aided by atmospheric pressure, and the contraction of the expiratory muscles. In how far muscle action is necessary for expiratory purposes will depend on the resistance offered to the outflow of air and on the degree of efficiency of the elastic forces.

Expiratory Center.—The simultaneous and coördinate activity of the expiratory muscles in impeded expirations also involves the action of motor nerves and nerve-centers. The simultaneous and coördinate discharge of nerve impulses, also graduated in intensity for expiratory needs, apparently implies the existence in the central nerve system of a single center from which nerve impulses are rhythmically discharged which excite and coördinate the lower nerve-centers. To this group of cells the term "expiratory center" has been given. The two centers taken together constitute the so-called "respiratory center."

The anatomic existence, however, of a definite group of cells which initiates the respiratory movements has not as yet been demonstrated. Nevertheless there is in the dorsal portion of the medulla oblongata, at the level of the sensory end-nucleus of the vagus nerve, a region the sudden destruction of which on one side is followed by a cessation of respiratory movements on the corresponding side, though they continue on the opposite side, a fact which indicates that the area, though acting as a unit, is bilateral. The bilateral character of the area is also shown by the continuance of the respiratory movements on both sides after longitudinal division of the medulla. Destruction of the entire region is followed by a complete cessation of respiratory activity and death of the animal. For this reason the term "nœud vital" (vital point) was applied to it. In this area the respiratory center was located. It has, however, been shown by Gad that if this area be gradually destroyed by cauterization the respiratory movements do not cease, but continue until the cauterization has reached a point far forward in the formatio reticularis, in which the respiratory center was assumed to lie.

Though its existence has not been anatomically determined beyond question, it is permissible to speak of the central mechanism as a "center" located in the medulla oblongata.

The Cause of the Rhythmic Activity of the Inspiratory Center.—It has long been a subject of discussion as to whether the periodic activity of the inspiratory center is automatic or autochthonic (Gad) in character, expressive of the idea that the rhythmic discharge of nerve impulses is due to some stimulating agent generated in the nerve-cells of the center itself, the activity of which is conditioned by the gaseous condition of the blood; or whether it is reflex in character, that is, due to the action of nerve impulses transmitted from different regions of the body through afferent nerves. The solution of this problem has apparently been settled by experiments the object of which was the division of all afferent nerve-paths that might have central connections with the center. The results of experiments of this character are somewhat as follows: When the vagus nerves are divided the respiratory movements at once diminish in number per minute but at the same time increase in depth and amplitude. The number of respiratory movements under these circumstances varies in different animals from four to eight per minute, a rate which continues practically constant so long as the animal lives, which may be a period varying from a few days to several weeks. The relative duration of the respiratory phases also undergoes a change, inspiration becoming longer than expiration and at the same time becoming more or less spasmodic in character.

Inasmuch as it is a familiar observation that the normal rate of the respiratory movement is frequently disturbed by nerve impulses transmitted to the center, through afferent nerves other than the vagi, as well as from higher centers in the brain, section of the vagi has been supplemented by a transverse section of the spinal cord at the level of the first dorsal nerve, by section of the dorsal roots of the cervical nerves and by a transverse section of the region of the brain just posterior to the corpora quadrigemina, a series of procedures which practically isolates the center from all transmitted impulses. Nevertheless, the inspiratory center still continues to discharge nerve impulses to the respiratory muscles at a rate not differing much from that witnessed after section of the vagi. At most the diminution in the rate will not be more than two or three more per minute. The results of these experimental procedures would seem to indicate that the fundamental rate of discharge of nerve impulses is approximately from four to six per minute. This conclusion has been strengthened by the results of experiments designed to suspend the activity for some minutes by the withdrawal of the blood by temporarily occluding the blood-vessels passing to the head. With the resuscitation of the center, after the release of the blood-stream and at a time when there are reasons for believing that the afferent paths are still incapable of conduction, the initial rate of discharge was practically constant, about four per minute in the cat. The same result was observed in some instances in cats when in addition to producing anemia the vagi as well as the region posterior to the corpora quadrigemina were divided (Stewart).

It may therefore be assumed that the respiratory center possesses an independent automatic rhythm which is, however, much slower than that characteristic of it when all afferent paths leading to it are intact.

Accepting the statement that the fundamental rhythm of the inspiratory center is automatic—that is, due to a stimulus generated within itself—the question at once arises as to the nature of the stimulating agent. By some investigators it has been assumed that the stimulus is connected with the content or pressure of oxygen, by others with the content or pressure of carbon dioxid, and that the variations in the respiratory rhythm are dependent on variations in the pressure of one or the other of these two gases. As a result of a long series of experiments made on animals and human beings, with the respiratory nerve mechanism intact, it is now the generally accepted opinion that the more efficient cause for the respiratory rhythm is an increase in the pressure of carbon dioxid in the blood and hence in the center itself rather than a decrease in the pressure of the oxygen. Whether the pressure of the carbon dioxid be the efficient cause or not of the fundamental respiratory rhythm, there is abundant evidence that the activity or the irritability of the center is modified to an extraordinary extent by variations in the pressure of the carbon dioxid when the nerve system is intact. Proofs in support of this statement will be given in a subsequent paragraph.

Reflex Stimulation of the Inspiratory Center.—Whether the inspiratory center is automatic in character or not, it may be influenced directly by nerve impulses descending from the brain in consequence of volitional acts or emotional states, and indirectly by nerve impulses brought to it from the general periphery through various afferent nerves, in consequence of agencies acting on their peripheral terminations: *e.g.*, cold applied to the skin, irritating gases to the nasal and bronchial mucous membrane, distention and collapse of the pulmonary alveoli.

The Relation of the Vagus Nerves to the Inspiratory Center.—The vagus nerves, of all the afferent nerves, appear to be the most influential in maintaining the normal rhythmic discharge of nerve impulses from the inspiratory center, as shown by the effects that follow their separation from the center. (Fig. 198.) Thus, if while the animal is breathing regularly and quietly both vagi are cut, the respiratory movements become much slower, falling perhaps to one-third their original number per minute. At the same time the inspirations become deeper and somewhat spasmodic in character. The duration of the inspiratory movement is also increased beyond that of the expiratory movement. If now the central end of one of the divided vagi be stimulated with weak induced electric currents, the respiratory movements are again increased in frequency and their depth diminished until the normal rate is restored. With the cessation of the stimulation the former condition at once returns. This would seem to indicate that the vagus nerve contains nerve-fibers which, under physiologic conditions, transmit nerve impulses which *inhibit* the inspiratory discharge and lead to an expiratory movement sooner than would otherwise be the case, and thus maintain the normal rate and extent of the inspiratory discharge. The stimulus to the development of these nerve impulses is generally believed to be the distension of the air cells at the beginning of the inspiratory movement.

If however the central end of the divided vagus be stimulated with induced electric currents of moderate intensity, the opposite effect is produced, viz.: an *increase* in the extent of the inspiratory movement and a decrease in the extent of the expiratory movement until the inspiratory muscles pass into the tetanic state and the chest walls come to rest in the condition of a forced inspiration. This would indicate that the vagus nerve also contains nerve-fibers which, with the proper degree of stimulation are capable of so exciting or augmenting the activity of the inspiratory center, and therefore the extent of the inspiratory movement, as to lead to the condition of tetanus of the inspiratory muscles. If, on the other hand, the central end of the divided superior laryngeal nerve be stimulated with induced electric currents, an effect the opposite of the foregoing is produced, viz.: a *decrease* in the extent of the inspiratory and an *increase* in the extent of the expiratory movement until the inspiratory muscles pass into the state of relaxation and the chest walls come to rest in the condition of complete expiration. This would indicate that the superior laryngeal nerve contains nerve-fibers which are capable, when sufficiently stimulated of *inhibiting* the activity of the inspiratory center, and therefore the extent of the inspiratory movement, as to lead to the condition of complete relaxation of the inspiratory muscles with a consequent expiratory standstill.

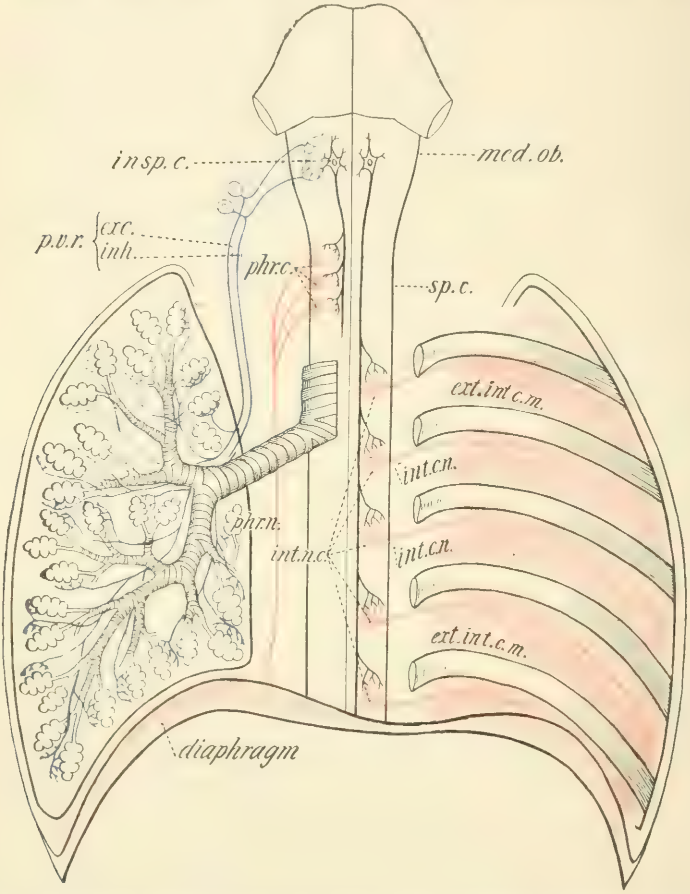

Fig. 198.—Diagram Showing the Relation of the Pulmonic Fibers of the Vagus to the Inspiratory Center and the Connections of the Latter with the Phrenic and Intercostal Nerve Centers and Their Related Muscles.—(*G. Bachman*). *med. ob.* Medulla oblongata. *sp. c.* Spinal cord. *p. v. r.* Pulmonic vagus nerve, excitator and inhibitor. *in sp. c.* Inspiratory center. *phr. c.* Phrenic nerve-centers. *phr. n.* Phrenic nerve. *int. n. c.* Intercostal nerve-centers. *int. c. n.* Intercostal nerves. *ext. int. c. m.* External intercostal muscles.

The same results, viz.: a complete relaxation of the inspiratory muscles leading to an expiratory standstill, not infrequently follows strong stimulation of the central ends of divided vagi, and always after the administration of large doses of chloral.

The results of these experiments would seem to indicate that the vagus nerve contains two classes of nerve-fibers, one of which, when stimulated with weak induced electric current, inhibits and regulates the discharge of nerve energy from the inspiratory center, and thereby the extent and frequency of the inspiratory movement; the other of which when stimulated, excites or augments the discharge of nerve energy from the inspiratory center and thereby leads to an increase in the depth or amplitude of the inspiratory movement. According as the one or the other of these two classes of fibers are excessively stimulated, will the inspiratory center be *inhibited* or *augmented* in its activity to such an extent that the chest walls will come to rest in the first instance in the state of expiratory standstill, in the second instance in the state of inspiratory standstill.

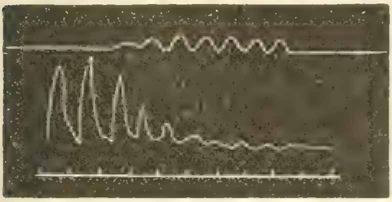

FIG. 199.—POSITIVE VENTILATION (*Head*). Under the influence of positive ventilation, the inspiratory contractions of the diaphragm become less and less till they disappear completely.

The stimulus adequate to the excitation of the pulmonic terminations of the vagus nerve-fibers in the physiologic condition was formerly believed to be the chemic action of carbon dioxid; it is now believed to be a mechanic action, the result of the alternate distention and collapse of the walls of the pulmonic alveoli. Thus, it has been shown by Head that if the lungs are actively inflated (positive ventilation) there will be produced an inhibition of the inspiratory and an augmentation of the expiratory movement until the inspiratory muscles are completely relaxed as indicated by the relaxation of the diaphragm, the movements of which are simultaneously recorded (Fig. 200), a result similar in all respects to that produced by stimulation of the superior larnygeal nerve. On the other hand, if the lungs are collapsed by the artificial withdrawal of air (negative ventilation) there will be produced an augmentation of the inspiratory and an inhibition of the expiratory movements until the inspiratory muscles are in a condition of tetanic contraction as indicated by the contraction of the diaphragm (Fig. 201) and by the state of the thorax which is that characteristic of extreme inspiration, a result similar in all respects to that produced by moderate stimulation of the central end of the divided vagus.

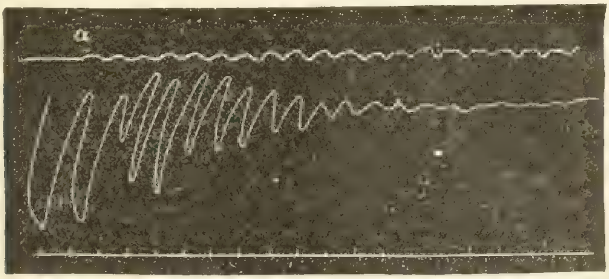

FIG. 200.—NEGATIVE VENTILATION. (*Head*). At *a* negative ventilation was commenced. The expiratory relaxation of the diaphragm is seen to become more and more incomplete, until it finally enters into continued contraction.

Theories of the Mode of Action of the Respiratory-nerve Mechanism.—A satisfactory explanation of the action of the respiratory-nerve mechanism is very difficult to present. Theories vary in accordance with the estimate of an investigator as to the degree of automaticity of the inspiratory center, of the effects of vagus stimulation and as to the extent to which the expiratory center is involved with the activity of the inspiratory center either simultaneously or successively.

The following theories have each found adherents.

1. If it is assumed that the inspiratory center is automatic and in a state of continuous excitation the result of the action of carbon dioxid in the blood circulating around it, then it is only necessary to assume the existence, in the trunk of the vagus of one set of nerve-fibers, viz.: *inhibitor* fibers, the central terminations of which arborize around the inspiratory center, and the function of which is to check or inhibit the discharge of the inspiratory center and thus permit of an expiratory movement. The inhibitor fibers are supposed to be stimulated peripherally by the expansion of the lungs. With the recoil of the lungs the inhibitor effect gradually dies away, while the inherent excitation of the inspiratory center again returns, to be followed by another discharge of nerve impulses and a new inspiratory movement, which will in turn be again inhibited as the inhibitor fibers are stimulated by the expanding lung. This explanation is in accordance with the results which follow stimulation of the superior laryngeal nerve or the trunk of the vagus with induced electric currents of slight intensity.

2. If it is assumed, on the contrary, that the inspiratory center is not in a state of constant excitation leading to a frequent periodic discharge of nerve impulses, but requires the arrival of a stimulus to call forth its normal activity, then this theory does not suffice, inasmuch as it leaves out of consideration the presence of nerve-fibers in the vagus which increase or augment the activity of the inspiratory center; and that such fibers are present is apparently indicated by the effects of stimulation of the central end of the vagus nerve with moderately strong induced electric currents, and from the experiments of Hering and Breuer, and later of Head. These observers assume, therefore, that in addition to the *inhibitor* fibers there are also present in the vagus *excitator* fibers, the central terminations of which are in relation with the inspiratory center also (Fig. 198); and just as the inhibitor fibers are stimulated by the expansion of the lungs, so the excitator fibers are stimulated in turn by the recoil of the lungs. The nerve impulses developed by the *recoil* of the walls of the alveoli ascend the vagus nerve to the inspiratory center, excite it to activity, and thus call forth a new inspiration sooner than it would otherwise take place. The nerve impulses developed by the *expansion* of the walls of the alveoli in turn ascend the vagus nerve to the inspiratory center and inhibit its activity and thus lead to an expiratory movement, sooner than it would otherwise take place. According to this view the respiratory mechanism is self-regulative and maintained by the alternate expansion and recoil of the lungs.

3. Another explanation which is satisfactory in many respects has been presented by Meltzer. This investigator asserts also the existence in the trunk of the vagus the two classes of nerve-fibers, the inhibitor and the excitator; but that for some reason they do not respond to stimulation at the same time as shown by the effects which follow; the inhibitor fibers

respond first and the excitator fibers somewhat later. Therefore when they are stimulated simultaneously the primary effect is an inhibition of the inspiratory center followed by an expiratory movement. The secondary effect is a stimulation of the inspiratory center followed by a new inspiratory movement. In this view expansion of the lungs stimulates both the inhibitor and the excitator fibers, but during the expansion and for a short time after, the effect of the inhibitor stimulation, viz.: cessation of inspiration and the advent of expiration, alone manifests itself. With the cessation of expiration, the inhibitor stimulation dies away and the late effect or the long after-effect of the excitator stimulation, viz.: a new inspiration, manifests itself. This investigator assumes the surface of the lung to be the peripheral organ of the respiratory reflexes.

When it is assumed that both inspiratory and expiratory centers coöperate in a respiratory movement, as they do in labored respiration either simultaneously or successively, the difficulties of the problem are manifestly much greater. In this case it may be supposed that afferent impulses, developed during the expansion of the lung, inhibit the inspiratory while augmenting the expiratory center, and that impulses developed during the recoil of the lungs inhibit the expiratory while stimulating the inspiratory center.

The Effect of a Change in the Pressure of the Blood Gases on the Activity of the Inspiratory Center.—It has long been known that the inspiratory center is very sensitive to a change in the composition of the blood in so far as its gaseous constituents are concerned. So long as the composition remains normal the center retains its normal irritability and rhythm. As stated in a previous paragraph it has been a subject of discussion as to whether the center is more responsive to an increase in the pressure of the carbon dioxid or to a decrease in the pressure of the oxygen. As the outcome of a long series of experiments it is now the generally accepted opinion that an increase in the percentage and pressure of the carbon dioxid in the blood and hence in the center itself is more efficient in raising the irritability of the center than a decrease in the percentage and pressure of the oxygen. Thus if an animal is caused to inhale air containing but 2 per cent. of CO_2 more than normal the respiratory movements will be increased in frequency and depth, while a corresponding diminution in the percentage of oxygen will be without effect.

It has been shown by Haldane and Priestley that when an individual was breathing normal air and the rate of the respiratory movement, 14 per minute, the average depth was 637 c.c. and the total ventilation was 8.918 liters per minute. On raising the percentage of the CO_2 in the inspired air from 0.04 per cent. to 0.79 per cent. the average depth increased to 739 c.c. and the total ventilation to 10.346 liters per minute, the rate remaining the same. When the percentage of the CO_2 was raised to 2 per cent. the average depth increased to 864 c.c., the rate to 15, and the total ventilation to 12.960 liters per minute; and when the CO_2 in the inspired air was raised to 6 per cent. the average depth was increased to 2104 c.c., the rate to 27 per minute, and the total ventilation to 56.808 liters. The results of these experiments indicate that an increase in the percentage of the CO_2 in the inspired air leads to an increase in the percentage and pressure of the CO_2 in the arterial blood and hence in the inspiratory center, as a result of which the center becomes more irritable and discharges its energy more frequently and to a greater degree as shown by the increase in the rate and the depth of the inspiratory movement.

The same observers have also shown that when an individual is caused to inhale air the percentage of the oxygen of which had been reduced from 20 to 13 and therefore to about 8 per cent. in the alveolar air instead of about 15 per cent. no particular change in either the frequency or the depth of the inspiratory movements was noticed, but when the percentage of the oxygen was lowered below this amount the inspiratory center became more irritable as shown by an increase in the rate and depth of the inspiratory movement. As a rule the oxygen percentage in the alveolar air must be reduced fully one-half and thereby the percentage and pressure of the oxygen in the arterial blood fully one-third before the respiratory center is stimulated to increased activity. A reason assigned for this result is the presence in the blood of some non-oxidized metabolic product, probably lactic acid, that is acting as the stimulus. All recent experimental work confirms the view that the specific stimulus to the inspiratory center is the normal pressure of the CO_2 in the blood and so responsive is it to this agent that an increase in even 0.2 per cent. in the alveolar air is sufficient to almost double the respiratory ventilation.

The Establishment of Respiration after Birth.—Previous to birth the exchange of the gases which constitutes the respiratory activity in the mammalian fetus, takes place in the placenta. The venous blood is carried by the umbilical artery to this organ in which the blood of the fetus comes into close relation with the blood of the mother, the two fluids being separated only by an extremely thin partition. The venous blood while passing through the placenta yields up its carbon dioxid to and receives oxygen from the maternal blood; after this exchange of gases the now-arterialized blood is returned to the fetus by the umbilical veins.

Immediately after birth and the detachment of the placenta, this method of gaseous exchange is abolished and if the life of the child is to be maintained the respiratory movement must be established. The cause of the first inspiration, therefore, must be associated with an increase in the percentage of carbon dioxid or a decrease in the percentage of oxygen in the blood. In accordance with statements in foregoing paragraphs the former condition is more likely to be the efficient cause. The rapid accumulation of carbon dioxid with its increasing pressure in the inspiratory center so raises its irritability as to lead to a discharge of nerve impulses which are conducted to the inspiratory muscles and cause their contraction. With the first inspiration thus established the nerve mechanism described, pages 424, 426 comes into play.

Inasmuch as cold water applied to the skin of the adult profoundly excites at times the inspiratory center it has been assumed that an additional factor leading to an excitation of the inspiratory center is the rapid cooling of the surface of the child by the evaporation of the amniotic fluid from the surface of the skin. The nerve impulses thus developed are transmitted through cutaneous nerves to the inspiratory center. This assumption is somewhat strengthened by the fact that in delayed inspiration the stimulation of the skin by the application of cold water frequently leads to a sudden inspiratory movement.

MODIFICATIONS OF THE RESPIRATORY RHYTHM

The rhythmic character of the respiratory movements is materially modified by a change in the quantitative and qualitative composition of the air and blood as well as by changes of a pathologic nature of the respiratory apparatus itself.

Eupnea.—So long as the air retains its normal composition and the respiratory mechanism its structural integrity, so long do the respiratory movements exhibit a normal rhythm and frequency. To the condition of easy tranquil breathing the term *eupnea* is given. In this condition the percentages of oxygen and carbon dioxid in the blood are such as to favor at least the rhythmic discharge of nerve impulses from the inspiratory center to the inspiratory muscles, of sufficient energy and frequency for the maintenance of normal respiration.

Hyperpnea.—The normal rate of the respiratory movements is increased by a rise in body-temperature, by active exercise, and by emotional states. Whatever the cause, the increase in rate and probably in depth is termed *hyperpnea.*

Febrile states characterized by a rise in the temperature of the blood increase considerably the respiratory activity. This is due in all probability to a warming of the inspiratory center, in consequence of which its irritability is heightened; for surrounding the carotid arteries with warm tubes and heating the blood on its way to the medulla has the same effect. It is also possible, however, that the high temperature of febrile conditions may interfere with the absorbing power of hemoglobin, and thus by diminishing the quantity of oxygen absorbed lead to more frequent respirations. To the hyperpnea induced by heat the term *thermo-polypnea* is frequently given.

Muscle activity, especially if it is violent and indulged in by those unaccustomed to exercise, is generally followed by increased rate and depth of breathing, and not infrequently it is attended with such extreme difficulty that the condition approximates that of dyspnea. This condition is attributed to the production and discharge into the blood of metabolic products which act as stimuli to the respiratory center and thus increase its activity. Of these metabolic products CO_2 is undoubtedly one of the most efficient, as stated in foregoing paragraphs. Emotional states temporarily increase respiratory activity. With their disappearance the normal condition returns.

Apnea.—Apnea may be defined as a temporary cessation of the respiratory movements. It may be developed by rapid and deep inspirations due to volitional efforts, by rapid mechanic inflation of the lungs, and by stimulation of various afferent nerves. If one volitionally breathes rapidly and deeply for a period varying from two to ten minutes, it will be found on cessation of the effort that a condition of apnea is established which may last for from thirty seconds to several minutes. One experimenter succeeded after forcible inspiration for two and a half minutes, in establishing in himself an apnea that lasted for several minutes before there was the slightest desire to breathe. Before the cessation of the apnea, the face became pale and corpse-like, indicative of a marked condition of anoxhemia. If the lungs of an animal be rapidly inflated through a cannula inserted in the trachea, a similar condition is developed. Whether the apnea be established by volitional efforts or by mechanic inflation, the respiratory movements gradually return. At first they are feeble but soon increase in amplitude and frequency until the normal is reached. At one time the apnea that results from rapid ventilation of the lungs, whether volitional or mechanical, was attributed, on the assumption that a deficiency of oxygen in the arterial blood is the physiologic stimulus to the activity of the inspiratory center, to an *excess* of oxygen in the blood, the result of the forced ventilation, complete saturation of the plasma and the hemoglobin, in consequence of which the inspiratory center remained inactive. The apneic state is at present attributed, on the assumption that carbon dioxid in the arterial blood is the physiologic stimulus to the inspiratory center, to a diminution in the percentage of the carbon dioxid in the alveolar air (to 4 per cent. or less), in the blood, and therefore in the center, the result of the forced ventilation. The increased ventilation eliminates the carbon dioxid to such an extent that the percentage and pressure in the blood is insufficient to arouse the center to activity. To the condition of the blood that results from this rapid ventilation, viz.: a diminished percentage of CO_2, the term *acapnia* has been given. An apnea which is thus developed is termed *apnea chemica* or *apnea vera.* As previously stated, stimulation of certain afferent nerves, especially the vagus, will induce a similar cessation of the respiratory movements. Thus if the central end of the divided vagus be stimulated with induced electric currents of marked intensity, the thorax will come to rest in the state characteristic of deep expiration from inhibition of the inspiratory center. Inasmuch as stimulation of the vagus causes an apnea resembling that caused by rapid inflation of the lungs, it has been suggested that in the development of apnea the inspiratory center is inhibited in its activity simultaneously with the elimination of the CO_2, from the mechanic stimulation of the pulmonic terminations of the vagus. An apnea caused by stimulation of the vagus is termed *apnea vagi* or *apnea inhibitoria.*

In the apnea that results from voluntary or mechanic inflation of the lungs it is difficult to state in how far the condition is due to a diminution in the pressure of the CO_2 and in how far to a stimulation of the vagus. But inasmuch as apnea can be established, though not of such long duration, after division of the vagus nerves, the probabilities are that the diminished percentage of the CO_2 is the main cause.

Dyspnea.—Excessive and laborious respiratory movements constitute a condition known as *dyspnea.* Movements of this character indicate that the blood contains a greater percentage of CO_2 than normal or a diminished percentage of oxygen. In either case the irritability of the inspiratory center is abnormally heightened. Of the two conditions, the former is by far the more common. While it is true that a deficiency of oxygen in the arterial blood gives rise to an increase in the rate and depth of the inspiratory movements, this does not arise until the deficiency of the oxygen falls to about one-third of the normal. On the other hand, an increase of even 0.2 per cent. of CO_2 in the alveolar air will almost double the inspiratory activity.

These conditions of the blood may be caused: (1) By all those pathologic conditions of the respiratory apparatus which limit the free entrance of oxygen into and the free exit of carbon dioxid from the blood; (2) by those alterations in the composition of the air and subsequently in the blood which arise when the individual is confined in a space of moderate size with imperfect ventilation. A deficiency in the amount or the quality of the hemoglobin is usually attended with more or less dyspnea.

Asphyxia.—If the state of the blood observed in dyspnea be exaggerated—that is, if the increase in the percentage of carbon dioxid become more marked—the respiratory movements become more laborious. A continuance of this changed composition of the blood eventuates in death. Before this occurs the individual exhibits a succession of phenomena, to the totality of which the term *asphyxia* is given.

Asphyxia may be caused: (1) By a sudden interference with the entrance of oxygen into and the exit of carbon dioxid from the blood, as in drowning, occlusion of the trachea from any cause, double pneumothorax, etc. (2) By confinement in a small space the air of which speedily undergoes a loss of oxygen and an accumulation of carbon dioxid. In the first instance death may occur in a few minutes; in the second instance it may be postponed several hours or more, the time varying with the size of the space.

The succession of phenomena presented by an individual in the asphyxiated condition is as follows: Increased rate and depth of the respiratory movements, passing rapidly from hyperpnea to dyspnea, with an active contraction of all the muscles concerned in respiration, ordinary and extraordinary; a blue, cyanosed condition of the face from the rapid accumulation of carbon dioxid and disappearance of the oxygen of the blood; a diminution in the depth of inspiration and an increase in the force and extent of expiration, followed by general convulsions; collapse, characterized by unconsciousness, loss of the reflexes, relaxation of the muscles, a weak action of the heart, a disappearance of the pulse, and death. As shown by observation of the circulatory apparatus in artificially induced asphyxia, there is primarily an increase in the activity of the heart, soon followed by retardation; a rise of blood-pressure in the early stages and a fall to zero after collapse has set in. The retardation and final cessation of the heart, as well as the rise of the blood-pressure, are to be attributed to stimulation of the cardio-inhibitory and vaso-motor centers from the accumulation of the carbon dioxid. With the exhaustion of the nerve-centers, there is a general relaxation of the skeletal muscles, the cardiac muscle, a fall of the blood-pressure, and dilatation of the pupils.

The Cheyne-Stokes Respiration.—A modification of the respiratory movements characterized by periods of rest alternating with periods of activity was described in 1818 and in 1854 by the two writers whose names it bears. The periods of rest vary in duration from twenty to thirty seconds; the periods of activity from thirty to sixty seconds and may include from twenty to thirty respiratory movements.

Each period of rest of the respiratory mechanism is closed by the appearance of a slight shallow respiratory movement, which is immediately followed by a second, slightly deeper, and this in turn by a third, a fourth, a fifth, and so on, each becoming deeper than the preceding until a certain maximum is reached, after which, each succeeding movement gradually diminishes in depth until finally the movement becomes imperceptible and a new period of rest supervenes. A graphic representation of the Cheyne-Stokes type of respiration is shown in Fig. 201. This type of respiration is frequently an accompaniment of certain pathologic conditions, *e.g.*, uremic states, cerebral hemorrhage, heart diseases, arteriosclerosis, etc., though no satisfactory explanation of it has yet been presented. A similar though far less marked periodicity in the respiratory movements is frequently observed during sleep, especially in children. A periodicity can also be developed by dividing transversely the medulla oblongata just above the calamus scriptorius, which either injures the respiratory center or removes from it some cerebral influence.

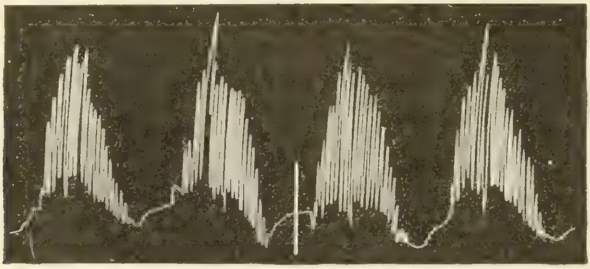

FIG. 201. —TRACING SHOWING THE CHEYNE-STOKES FORM OF RESPIRATION.—(*Hill.*)

THE EFFECT OF THE RESPIRATORY MOVEMENTS ON THE FLOW OF BLOOD THROUGH THE INTRA-THORACIC VESSELS, AND ON THE ARTERIAL PRESSURE

1. On the Intra-thoracic Vessels.—The forces which cause the air to flow into and out of the lungs will at the same time and in a similar way cause the blood of the extra-thoracic veins to flow into, through, and out of the intra-thoracic vessels. From the tendency of the pulmonic elastic tissue to recoil, the blood-vessels in the thorax at the end of an expiration sustain a positive pressure, the intra-thoracic pressure (see page 305), about six millimeters of mercury less than that in the lungs, or, in other words, a pressure negative to that of the atmosphere by six millimeters. As a result the blood in the systemic vessels under atmospheric pressure will flow steadily toward the intra-thoracic veins, the venæ cavæ, and the right side of the heart, *i.e.*, from a point of high to a point of low pressure. During inspiration there is a decrease in the intra-thoracic pressure, the decrease being proportional to the extent of the inspiration. With this decrease of pressure, the intra-thoracic veins expand and their internal pressure falls. As the systemic or extra-thoracic veins are subjected to atmospheric pressure, the blood in these vessels is forced, by reason of the difference of pressure between these two regions, to flow more rapidly and freely into the intra-thoracic veins and right side of the heart. The right heart being more generously filled with blood will discharge a larger volume with each contraction into the pulmonic artery.

Coincident with these effects a similar effect is produced in the arterioles and capillaries of the pulmonic alveoli. Situated between the two elastic layers of the alveolar wall, embedded in a meshwork of connective tissue, the pressure to which they are subjected at the end of an expiration will also be a few millimeters less than the intra-pulmonic pressure; and at the end of an inspiration it will be considerably less. With the inspiration therefore there will occur a dilatation of these vessels, and hence a larger flow of blood through them and into the pulmonic veins. The left heart, being in consequence more generously filled with blood, will discharge a larger volume into the aorta at each contraction. During expiration the flow of blood through the intra-thoracic vessels will be diminished for the reverse reasons.

2. **On the Arterial Pressure.**—An examination of a tracing of the arterial pressure will show that it is characterized by small undulations due to the cardiac beat and large undulations due to the respiratory movements, inspiration being accompanied by a rise, expiration by a fall of pressure. These results are readily accounted for by the difference in the volume of blood discharged by the left heart into the aorta during the time of the two movements. If a tracing of the respiratory movements and of the blood-pressure be taken simultaneously, it will be found that the rise of pressure does not exactly correspond with inspiration, nor the fall of pressure with expiration; for a certain period after the beginning of an inspiration the pressure continues to fall, and for a certain period after the beginning of an expiration the pressure continues to rise. During the remainder of the period, however, inspiration is attended by a rise, expiration by a fall of pressure. The explanation of these results lies in the fact that at the beginning of the inspiration, when the vessels dilate, the blood-flow momentarily slows; the left heart continuing to discharge small volumes into the aorta, the pressure continues to fall. So soon as the left heart begins to be better filled, the pressure at once begins to rise. At the end of an expiration the flow of blood into the left heart continues and the pressure rises, but with the return of the intra-thoracic pressure the vessels diminish in caliber, the volume of blood transmitted by them becomes less, the output of the left heart declines, and the pressure falls.

3. **On the Flow of Lymph.**—The fall of the intrathoracic pressure during an inspiratory movement has an accelerating effect on the flow of lymph from the abdominal portion of the thoracic duct into the thoracic portion. The rise of the pressure during an expiratory movement causes a more abundant discharge of lymph from the end of the duct, into the venous blood. The advantages of this mechanism have been alluded to on page 225.

CHAPTER XVI

ANIMAL HEAT

The animal body possesses a temperature that is perceptible to the sense of touch and determinable by a thermometer. This temperature is the result of the liberation of heat which attends the chemic changes taking place in the tissues and organs of the living body and which underlie all manifestations of life. In consequence of this each animal acquires a certain body-temperature.

In man, as well as in other mammals and in birds, the chemic changes are extremely active and the evolution of heat very great. Through some special heat-regulating mechanism, by which heat-production and heat-dissipation are kept in equilibrium, these animals have acquired and maintain within limits a constant temperature which is independent of and generally above that of the surrounding atmosphere. As the temperature of these animals is high and perceptible to the sense of touch, they were originally designated "warm-blooded" animals. As this temperature is constant notwithstanding the great variations in external temperature during the summer and winter seasons, they are more appropriately termed constant-temperatured or *homoio-thermous* animals. The intensity of the body-temperature determined by the insertion of a thermometer in the rectum varies in different classes of mammals from 37.2°C. to 40°C. The causes of this variation are doubtless connected with peculiarities of organization. In birds the rectal temperature is usually higher, varying from 40.9°C. in the pigeon to 44°C. in the titmouse and the swift.

In reptiles, amphibians, and fish, chemic changes as a rule are not very active and heat-production relatively slight. As they are devoid of a sufficiently active heat-regulating mechanism, the temperature of the body is largely dependent on that of the medium in which they live, though it is always one or more degrees above it. In winter the body-temperature of frogs, for example, may decline as low as 8.9°C., the temperature of the surrounding medium being 6.7°C. When subjected to temperatures below zero, the temperature of the body may fall below the freezing-point also, when the lymph and fluids of the body become ice. Though apparently dead, the gradual elevation of the temperature restores their vitality. In summer-time, on the contrary, the body-temperature may attain to 38°C. Similar variations have been observed in other animals. As the temperature of these animals is low and perceptibly below that of our own bodies, they were originally termed "cold-blooded" animals; as their temperature is inconstant, varying with the temperature of the surrounding medium, they are more appropriately termed "variable-temperatured" or *poikilo-thermous* animals.

THE TEMPERATURE OF THE HUMAN BODY

The determination of the temperature of the human body under the changing conditions of life is a matter of the greatest physiologic and clinical interest. The temperature of the superficial portions of the body may be obtained by the introduction of a thermometer into the mouth, the rectum, the vagina, or the axilla. As a result of many observations it has been found that the temperature of the rectum is, on the average, 37.2°C.; that the mouth, 36.8°C.; that of the axilla, 36.9°C. Owing to radiation and conduction, the surface temperature is lower than that of either the mouth or rectum, and varies to a slight extent in different regions of the body: *e.g.*, at a room-temperature of 20°C. the skin of the pectoral region has a temperature of 34.7°; that of the cheek, 34.4°; that of the calf, 33.6°; that of the tip of the ear, only 28.8°, etc.

In the interior of the body, especially in organs in which oxidation takes place rapidly, and which at the same time are protected by their anatomic surroundings from rapid radiation, the temperature is higher than that observed in the rectum. From an investigation of the temperature of the blood as it emerges from the liver, the muscles, the brain, alimentary canal, etc., it is evident that these organs have a higher temperature than the rectum.

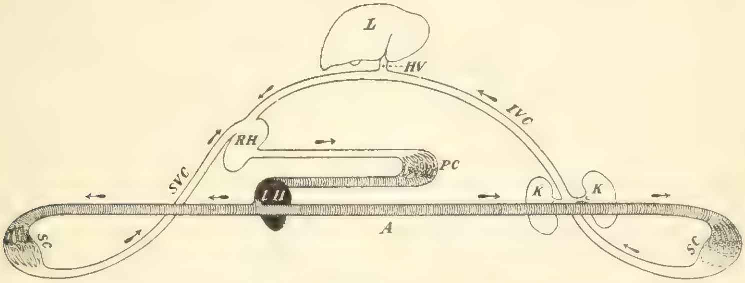

FIG. 202.—SCHEME TO SHOW THE TOPOGRAPHIC DISTRIBUTION OF THE TEMPERATURE IN THE LARGE BLOOD-VESSELS. The degree of temperature in these vessels is expressed at each point by its height above a conventional abscissa which is here the aorta, in which the temperature is practically uniform.—*(After Bernard.)*

As the chemic changes underlying physiologic activity vary in intensity and extent in different regions of the body, there would be marked variations in their temperature were it not that the blood, having a large capacity for heat-absorption, distributes the heat almost uniformly to all portions of the body, so that at a short distance beneath the surface the temperature varies but a few degrees.

In the dog the temperature of the blood in the aorta and in its principal branches is approximately 38.6°C. In passing through the systemic capillaries the temperature falls from radiation and conduction to surface temperature, to again rise as the venous blood approaches the deeper regions of the body (Fig. 202). In the neighborhood of the renal veins and in the superior vena cava, the temperature is again that of the aorta. In the portal vein the temperature rises to 39°C.; in the hepatic vein, to 89.7°C. In the right ventricle, owing to the admixture of blood from different localities having different temperatures, the temperature falls to 38.8°C In passing through the pulmonic capillaries the temperature of the blood again falls, so that in the left ventricle it will register 38.6°C. There is thus usually a difference between the two sides of the heart of about 0.2°C.

Variations in the Mean Temperature.—The mean temperature of the human body for twenty-four hours, which for the mouth and the rectum may be accepted at 36.8°C. and 37.2°C. respectively, is subject to variations from a variety of circumstances, such as age, periods of the day, food, exercise, etc.

Age.—At birth the temperature of the infant is slightly higher than that of the mother, registering in the rectum about 37.5°C. In a few hours it rapidly declines to about 36.5°, to be followed in the course of twenty-four hours by a rise to the normal or slightly beyond. During childhood the temperature gradually approximates that of the adult. In old age the temperature rises, as a rule, and attains a maximum at eighty years of 37.4°C.

Periods of the Day.—The observations of Jürgensen show that there is a diurnal variation in the mean temperature of from 0.5°C. to 1.5°C., the maximum occurring late in the afternoon, from 5 to 7 o'clock, the minimum early in the morning, from 4 to 7 o'clock. This diurnal variation in the mean temperature is related to corresponding variations in many other physiologic processess, and its causes are to be found in the ordinary habits of life as regards the time of meals, periods of exercise, sleep, etc.

Food and Drink.—The ingestion of a hearty meal increases the temperature but slightly—not more than 0.5°C. Insufficiency of food lowers the temperature; total withdrawal of food, as in starvation, is followed by a steady though slight decline, until just preceding the death of the animal, when it falls abruptly to from 6° to 8°C. Cold drinks lower, hot drinks raise the temperature. Food and drinks, however, only temporarily change the mean temperature, and after a short period equilibrium is restored through the activity of the heat-regulating mechanism. Alcoholic drinks lower the temperature about 0.5°C. In large toxic doses in persons unaccustomed to their use the temperature may be lowered several degrees. This is attributed not to a diminution in heat-production, but rather to an increase in heat-dissipation (Reichert) from increased action of the heart, dilatation of the blood-vessels of the skin, and increased activity of the sweat-glands.

Exercise.—The temperature may be raised by active muscular exercise from 1° to 1.5°C. as a result of increased activity in chemic changes in the muscles themselves. A rise beyond this point is prevented by the increased activity of the circulatory apparatus, the removal of the heat to the surface, and its rapid radiation.

External Temperature.—The external temperature influences but slightly the mean temperature of the human body. In the tropic, as well as in the arctic regions, notwithstanding the change in the temperature of the air, the temperature of the body remains almost constant. The same is true for the seasonal variations in the temperature of the temperate regions.

The Residual Heat of the Body.—As a preliminary to a consideration of heat-production and heat-dissipation, it is of interest to determine the actual quantity of heat expressed in Calories, that resides in the body at all times. This can be approximately determined from the chemic composition and the temperature. A chemic analysis of the body shows that it consists of water 0.6, and of tissue 0.4. If the weight be assumed to be 70 kilograms then 42 kilograms consist of water, and as the temperature is 37°C., the 42 kilos of water will contain 42 × 37 or 1554 kilogram calories;

the remaining 28 kilograms consist of tissues, the specific heat of which is but 0.8 that of water, hence the 28 kilograms of tissue will contain 28 × 0.8 Calories, the equivalent of 22.4 kilograms of water. Since the temperature of the body is 37°C. the additional number of Calories will be 22.4 × 37 or 828, making a total of 2382 Calories an amount of heat absolutely necessary to maintain the body-temperature at the physiological level. Notwithstanding the constant liberation of large amounts of heat each day, it is dissipated more or less rapidly in accordance with variations in temperature, character of clothing and a variety of other conditions, and so accurately is this done, that at the end of the twenty-four hours the body possesses its customary quantity of heat and its physiologic temperature.

HEAT-PRODUCTION. THERMOGENESIS

The Source of Heat.—The immediate source of the body-heat is to be found in the chemic changes which take place in all the tissues and organs of the body. Each contraction of a muscle, each act of secretion, each exhibition of nerve-force, is accompanied by the evolution of heat. The chemic changes are for the most part of the nature of oxidations, the union of oxygen with the elements, carbon and hydrogen, of the food principles either before or after they have become constituents of the tissues. The ultimate source of the body-heat is the latent or potential energy in the food principles, which was absorbed from the sun's energy and stored up during the growth of the vegetable world. In the metabolism of the animal body the food principles are again reduced through oxidation, directly or indirectly, to relatively simple bodies, such as urea, carbon dioxid, and water, with a liberation of a large portion of their contained energy which manifests itself as heat and mechanic motion.

The Total Quantity.—The total quantity of heat liberated in the body daily may be approximately determined in at least two ways: (1) By determining experimentally the heat values of different food principles by direct oxidation; (2) by collecting and measuring with a suitable apparatus, a calorimeter, the heat evolved by the oxidation of the food within, and dissipated from, the body daily.

1. *Direct Oxidation.*—The amount of heat which any given food principle will yield can be determined by burning a definite amount—*e.g.*, 1 gram—to carbon dioxid and water and ascertaining the extent to which the heat thus liberated will raise the temperature of a given amount of water, *e.g.*, 1 kilogram. The amount of heat may be expressed in gram or kilogram degrees or calories; a gram calorie or kilogram calorie being the amount of heat required to raise the temperature of a gram or a kilogram (1000 grams) of water 1°C. The apparatus employed for this purpose is termed a calorimeter, which consists essentially of a closed chamber, in which the oxidation takes place, surrounded by a water-jacket. The rise in temperature of the water indicates the amount of heat produced.

The results obtained by investigators employing different calorimeters and different food principles of the same class vary, though within narrow limits: *e.g.*, 1 gram casein yields 5.867 kilogram calories; 1 gram of lean beef, 5.656; 1 gram of fat, 9.353, 9.423, 9.686 Calories; 1 gram of starch or sugar, 4.116, 4.182, 4.479, etc., Calories. These results are, however, physical values, and indicate the quantity of heat such quantities of foods give rise to when completely oxidized to carbonic acid and water. In the animal body the carbohydrates and the fats, with the exception of the small portion which escapes digestion, are reduced to carbon dioxid and water, and hence practically liberate as much heat as they do when oxidized outside the body. The proteins, however, are only reduced to the stage of urea. As this compound is capable of further reduction in the calorimeter to carbon dioxid and water, with the liberation of heat, the quantity of heat it contains must therefore be deducted from the physical heat value of the protein. According to Rubner, 1 gram of urea will yield 2.523 kilogram calories. As about one-third of a gram of urea results from the oxidation of 1 gram of protein, the amount of heat to be deducted from the heat value of the protein is $\frac{1}{3}$ of 2.523, or 0.841 Calories. It has also been shown by the same investigator that some of the ingested protein is found in the feces, the heat value of which must also be determined and deducted. This having been done, the physiologic heat value of protein thus becomes 4.124 Calories.

The following estimates give approximately the number of kilogram calories which should be liberated within the body when the protein is burned to the stage of urea, and the fat and carbohydrate to the stage of carbon dioxid and water:

1 gram of protein	4.124 Calories
1 gram of fat	9.353 Calories
1 gram of carbohydrate	4.116 Calories

The total number of kilogram calories yielded by the various diet scales can be readily determined by multiplying the quantities of the food principles consumed by the foregoing factors.

2. *Calorimetric Measurements.*—It has been determined from a long series of experiments that the animal body dissipates a variable amount of heat from day to day, an amount that can be collected and measured by placing the animal in a suitable apparatus—a calorimeter. A calorimeter is therefore an apparatus designed for the direct determination of the quantity of heat dissipated from the body in any given time. The amount obtained by this method expressed in Calories is taken as a measure of the heat liberated by the oxidation of the food, providing of course, the temperature of the animal remains unchanged. The substance employed for collecting and measuring the heat is usually water. The calorimeters in general use consist essentially of two metallic boxes placed one within the other, though separated by a space sufficiently large to hold a definite amount of water (Fig. 203). The animal is placed in the inner box, which is also provided with tubes for the entrance of fresh and the exit of expired or vitiated air. The heat radiated is absorbed by the water and its temperature raised. To prevent loss by radiation and to render it independent of changes in the surrounding temperature the calorimeter is surrounded by a poorly conducting material, such as wool. The temperature of the animal is taken at the beginning and the end of the experiment. If the temperature of the animal remains the same at the end of the experiment, then the heat absorbed by the water represents the amount produced by the animal. If, on the contrary, the temperature of the animal rises or falls, the number of calories so retained or lost must be added to or subtracted from the amount absorbed by the calorimeter. In the determination

of the absolute amount of heat retained or lost by the animal above or below the initial temperature, as well as that absorbed by the materials of the apparatus in these various instances, the water equivalent of the tissues of the animal and the materials of the calorimeter must be obtained, and then added to or subtracted from, as the case may be, the amount of water in the calorimeter, and the amount thus obtained multiplied by its rise in temperature.

When means are taken to collect for purposes of analysis, the urine and the feces and also the expired air, the apparatus is designated a respiration calorimeter. The nitrogen in the urine and feces and the carbon dioxid in the expired air permit of the determination of the amounts of protein and fat metabolized. The ventilation of the chamber is accomplished by some form of aspirating apparatus.

In properly conducted experiments in which the sources of error are reduced to a minimum there is a very close correspondence between the total physiologic heat value of the food and the amount collected by the calorimeter. Thus, in an experiment detailed by Rubner, a dog was given during twelve days 228.06 grams of protein and 340.4 grams of fat, the physical heat value of which was estimated at 4429 Calories. The urine and feces during this period were collected and their heat value determined, which amounted to 305 Calories. The heat which theoretically therefore, should have been produced was 4124 Calories. During the experiment the calorimeter actually absorbed 3958 Calories, a difference between the theoretic and experimental results of 166 Calories; thus of the total energy liberated about 96 per cent. appeared as heat.

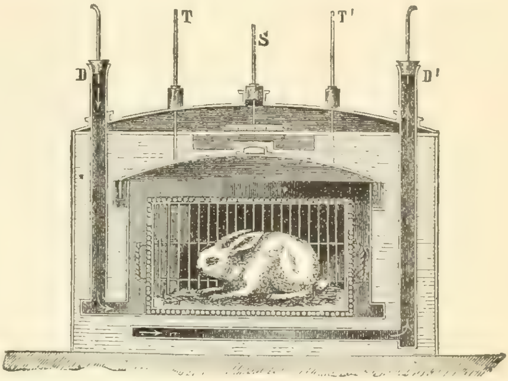

FIG. 203.—WATER CALORIMETER OF DULONG. D and D′. Tubes for the entrance and exit of air. T and T′. Thermometers for ascertaining the temperature of the water. S. A mechanic contrivance for stirring the water for the purpose of distributing the absorbed heat uniformly. To prevent the escape of heat with the expired air, the tube D′ is wound many times in the water-space beneath the animal cage.

Calorimetric experiments on human beings corresponding in general to those made on dogs and other animals, have been made possible in recent years by the employment of the ingenious and finely constructed respiration calorimeters devised by Atwater, Benedict and their co-workers. With these forms of apparatus the same close correspondence between the amount of heat actually absorbed by the calorimeter and the amount which theoretically would be liberated by the oxidation of the food, has been found to hold true. Inasmuch as the calorimeter of Benedict differs in some respects from those hitherto employed, a brief description of the principle on which it is constructed may not be inappropriate. The calorimeter chambers, though sufficiently large to accommodate a human being, vary in size and general arrangement in accordance with the character of the experiment. The construction of each however is essentially the same.

These calorimeters consist of two parts, one for the collection of the heat liberated by the subject of the experiment, and the other for the collection of the carbon dioxid and water exhaled and for the measurement of the oxygen consumed. Means are also provided for the collection of the urine and feces when necessary.

The first part of the calorimeter consists, Fig. 204, of a chamber of sufficient size with metallic walls, copper and zinc so arranged as to prevent either absorption or radiation of heat, in other words that they will be heat-proof. At one side there is a door of sufficient size to admit the subject as well as a window to admit light. The heat dissipated by the subject of the investigation is taken up by a current of water of even but low temperature and flowing constantly under a steadily acting pressure through a copper pipe of 6 mm. internal and 10 mm. external diameter. The temperature of the water is determined before it enters and after it leaves the chamber. The amount of water passing through the tube in a given time, is collected and weighed. The difference in temperature, multiplied by the weight of the water gives the amount of heat dissipated by the individual. To facilitate the absorption of the heat a large number of copper discs 5 centimeters in diameter are soldered to the water pipe at a distance of 5 millimeters from one another. As the absorption pipe is some 5 meters in length, the area presented for absorption approximates about 4.7 square meters. The heat thus absorbed is soon conducted to the water followed by a rise in its temperature. Inasmuch as many experiments extend over a period of several days or more, special arrangements have been devised for the introduction of food which do not interfere with the accurate working of the calorimeter. The door of the food aperture is provided with glass for the transmission of light into the chamber. In some calorimeters a bed is provided, in others a chair as well as devices which enable the subject to perform a measurable quantity of mechanical work.

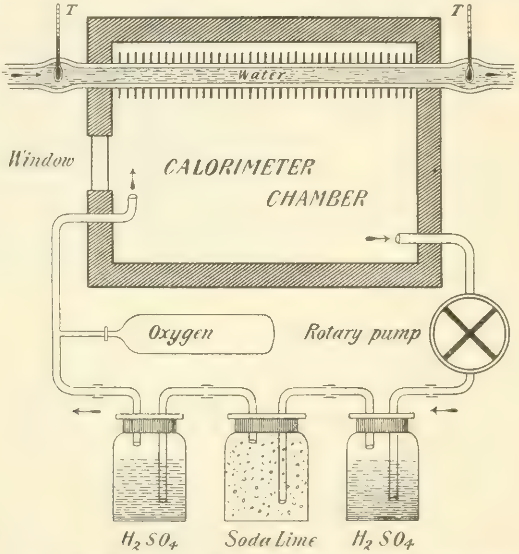

FIG. 204.—DIAGRAM TO SHOW THE PRINCIPLE OF THE ATWATER-BENEDICT CALORIMETER.

The second part of the calorimeter consists of a closed system of tubes and absorption vessels through which the air is kept moving under the action of a blower and thus kept in a respirable condition. As the air leaves the chamber it passes through two absorption vessels by which the water and carbon dioxid are successively absorbed and collected by sulphuric acid and soda lime respectively. The air then passes through an additional sulphuric-acid vessel which absorbs any water carried from the soda-lime vessel by the air and so back into the chamber. By weighing these absorbing vessels before and after the experiment the amount of water and carbon dioxid are readily determined. The oxygen of the air of the chamber that is utilized for respiration purposes is restored by the admission of oxygen from a cylinder in necessary amounts by special automatic devices. The amount of oxygen entering the chamber is determined by weighing the cylinder before and after the experiment. The loss in weight shows the oxygen consumed. Of course, the air of the chamber must be analyzed to correct certain errors that may possibly arise.

With the calorimeters described in the foregoing paragraphs it is possible not only to determine *directly*, but also *indirectly*, from the amounts of protein, fat, and carbohydrate metabolized (calculated from the C,H,O, and N eliminated and O absorbed) the heat produced and dissipated each day under a great variety of conditions *e.g.*, when the subject is fasting or living on the customary diet; when resting or doing a fair days work; when in health or in disease, etc.

1. *During Fasting.*—In an experiment extending over a fasting period of seven days' duration, recorded at length by Benedict, the heat was determined directly, and also indirectly, from the materials metabolized. Some of the results of this experiment are shown in the following tables:

METABOLISM OF S. A. B. DURING A SEVEN-DAY FAST

Day	Calories				Grams			R. Q.	Urine	
	Directly Determined	Calculated from Metab.	Per Kg.	Per Sq. M.	Protein	Fat	Glycogen		Ratio N : S.	Ratio $N:P_2O_1$
1	1765	1796	29.7	941	73.4	126.4	64.9	.78	19.6	8.55
2	1768	1790	29.9	946	74.7	147.5	23.1	.75	18.6	5.55
3	1797	1785	30.8	969	78.1	153.0	5.4	.74	17.38	6.34
4	1775	1734	30.8	966	69.8	144.7	25.2	.75	16.11	4.83
5	1649	1636	29.0	985	65.2	144.7	8.2	.74	16.26	5.23
6	1553	1547	27.5	856	64.4	129.8	21.7	.75	16.27	5.19
7	1568	1546	28.0	869	60.8	132.5	18.7	.74	16.28	4.87

Many similar experiments have been made by Benedict and by others with different forms of apparatus. As an average result it may be stated that in the fasting condition and doing light work there is an average heat-dissipation of 31 or 32 calories for each kilogram of body-weight, thus making a total for a man weighing 70 kilograms of 2170 or 2240 Calories.

2. *On the Customary Diet.*—When an individual is supplied with the food materials composing a customary diet, and is therefore in the physiological condition, the amount of heat produced and liberated is necessarily in-

creased. Under these circumstances there will be an increase of from 10 to 14 per cent. thus raising the heat-production and dissipation per kilogram of body-weight from approximately 32 Calories to 35.5 or 36.5 or a total of 2485 to 2555 Calories. The heat liberated by the metabolism during inanition is not sufficient to maintain the body in heat equilibrium and therefore, an increase in the food supply of from 10 to 14 per cent. beyond that metabolized is necessitated. A reason assigned for this necessity is as follows: During digestion and in the earlier stages of assimilation, the foods undergo a reduction and cleavage, in consequence of which a portion of their contained energy is liberated as free heat which however cannot be utilized by tissue cells in the performance of their various activities. This heat is probably directly dissipated in an environment of 33°C. The energy that cells require for the manifestations of their physiologic activities must apparently be derived only from the metabolism of food materials within themselves. Therefore, food materials in amount just sufficient to replace the amount metabolized in inanition, would furnish an amount of heat which would be insufficient to maintain the body in heat equilibrium. Though this holds true for a man weighing 70 kilograms it is not strictly true for men who weigh less or have a different skin area. It has been pointed out by Rubner that the number of Calories dissipated per kilogram of body-weight varies with the weight and the skin area: that the metabolism is proportional to the surface area or, in other words, whatever the weight, there will be for a given surface area, a certain heat loss leading in turn to a given metabolism of food materials. In the following table the weights of different men, their skin areas, total heat-production as well as Calories per kilogram while doing light work are presented. (Rubner.)

Weight in Kg.	Area in Sq. M.	Calories of Metabolism.	Calories per Kg.
80	2.283	2864	35.8
70	2.088	2631	37.7
60	1.885	2368	39.5
50	1.670	2102	42.0
40	1.438	1810	45.2

In the foregoing table it will be observed that in the man weighing 80 kilograms, the ratio of skin area to kilogram is 0.0285, while in the man weighing 40 kilograms the ratio is 0.0359. The heat liberated by this slight increase in skin area amounts to 9.4 calories per kilogram weight.

3. *During Work.*—The foregoing estimates as to the amounts of heat produced have reference mainly to the body in repose. When the body passes into a state of muscle activity, there is at once a notable increase in heat-production in consequence of the increase in the activity of the chemic changes which underlie body activity, as shown by the increase in the consumption of oxygen and the production of carbon dioxid. Not all of the potential energy set free, however, appears as heat; for, if the muscles are engaged in doing work a part of the energy, which would otherwise manifest itself as heat is converted into mechanic motion. From the work done during a period of eight hours it has been estimated that about 500 calories are so transformed or utilized. Hirn calculated from an average of five experiments that a man weighing 67 kilos in repose produced 154.4 calories per hour and absorbed 30.7 grams of oxygen per hour; but

when engaged in active muscle movements produced 271.2 calories and absorbed 119.84 grams of oxygen per hour. The increase in heat-production per hour during activity was thus almost doubled, though the sum total produced daily in which there was a working period of eight or ten hours was only about one-third more than during a day of repose. During sleep there is a greatly diminished heat-production, not more than 40 calories per hour being produced. The preceding data may be tabulated as follows (Hirn):

	Day of Rest.		Day of Work.		
	Rest 16 hrs.	Sleep 8 hrs.	Rest 8 hrs.	Work 8 hrs.	Sleep 8 hrs.
Heat units (Calories) produced	2470.4	320	1235.2	2169.6	320
	2790.4		3724.8		

Increased muscle activity is associated with increased metabolism and a more rapid dissipation of heat, which must be compensated for by a corresponding heat-production if heat equilibrium is to be maintained. This necessitates a larger amount of food ingested. From Calorimetric investigations, as well as from a calculation based on the amounts of the excreted products, various diet scales have been arranged by different investigators, which it is believed will furnish the extra amount of energy. A few are here appended.

DIETARIES FOR A MAN OF 70 KILOS, DURING HARD WORK

	Voit.	Rubner.	Playfair.	Hultgren.	
Protein	145	165	155	134	grams
Fat	100	70	70	79	grams
Carbohydrate	500	565	567	522	grams
	3574	3362	3619	3436	Calories

The Mechanism of Heat-production.—Heat is liberated to a greater or less degree in all tissues in the cells of which food materials are undergoing disruption and oxidation or metabolism. The tissues in which metabolism and therefore heat liberation takes place most energetically, e.g., muscles and glands are more especially to be regarded as thermogenic tissues.

Heat-production varies in intensity and amount, in accordance with a number of conditions, but principally with variations in physiologic activity, the quantity and quality of the food, and changes in the external temperature.

It will be recalled that all muscles possess tonicity by which is meant a slight degree of contraction, the result of the continuous arrival of nerve impulses through efferent nerves discharged from motor nerve-cells in the spinal cord this discharge being maintained largely by nerve impulses coming through afferent nerves from the muscles themselves, the joints, tendons, and skin. As a result of this slight but constant stimulation of the spinal cord, the metabolic changes in muscle material are maintained at a certain level, with a corresponding liberation of heat. The chief result of the tonicity would thus be the production of heat. Any physiologic condition that leads to a greater discharge of nerve impulses from the spinal cord and hence increased muscle activity, must be attended by increased heat-production. Therefore work and exercise of all kinds which involve a more rapid contraction of the skeletal muscles is attended with increased heat-production. By reason of their mass and more or less continuous activity the muscles are justly regarded as the chief thermogenic organs.

The consumption of foods that have a higher potential heat value also contribute to the amount of heat produced. Foods have different physiologic heat values. If the food consumed contains much potential energy and quantity consumed be larger than the average daily requirements, there will be an increase in heat-production. (See page 442.)

The chief external factor that increases metabolism in these and other organs and tissues is a low external temperature. A fall of the external temperature, such as is experienced in the fall and winter seasons, causes, through cutaneous afferent nerve stimulation, a stimulation of the spinal motor centers, and to a larger discharge of nerve impulses to muscles, glands, and other tissues. The increased metabolism thus developed leads to the consumption of increased amount of food and oxygen. As a result there is an increased heat-production. If at the same time volitional activities of muscles be evoked, as is not infrequently the case, there will be a still further increase in metabolism and heat liberation. When all these conditions, increased muscle activity, increased amount of food with high potential energy, and a low external temperature coexist, heat-production attains its maximum, amounting to as much as 4726 Calories daily (Hultgren).

HEAT-DISSIPATION. THERMOLYSIS

From the preceding statements it is evident that the body is continually liberating heat in amounts daily, far in excess of that necessary for the maintenance of the body-temperature. Should this heat be retained, the temperature of the body would be raised at the end of twenty-four hours, an additional 18° or 20°C.—a temperature far in excess of that compatible with the maintenance of physiologic processes. That the body may be kept at the mean temperature of 37°C. it is essential that the heat liberated be dissipated as fast as it is produced, or to state the problem in another way, the heat dissipated by the body must be replaced by an equal amount liberated, if equilibrium of temperature is to be maintained. The dissipation of the heat is accomplished in several ways: (1) In warming the food and drink to the temperature of the body. (2) In warming the inspired air to the same temperature. (3) In the evaporation of water from the lungs. (4) In evaporating water from the skin. (5) In radiation and conduction from the skin. The quantities of heat lost to the body by these different processes it is difficult for obvious reasons to accurately determine, and the estimates usually given must be regarded only as approximative.

The number of Calories which are theoretically liberated by the various diet scales can be readily determined by multiplying the quantities of food principles consumed by the usual factors (see page 442). Thus the total number of Calories furnished by the various diet scales would be as follows: Voit's, 3387; Vierordt's, 2695; Ranke's, 2335; Moleschott's, 2984; Atwater's, 3331; Hultgren's, 3436. As the body-weight may not increase and as the temperature in physiological conditions does not rise, the assumption is that the food is oxidized in the body to urea, carbon dioxid and water with the liberation of the foregoing amounts of heat and their equally rapid dissipation.

Assuming 2500 Calories to be an average of heat liberated during a day of repose, the losses, in the ways stated in the foregoing paragraph, may be tabulated as follows:

1. *In Warming Food and Drink.*—The average temperature of food and drink is about 12°C.; the amount of both together is about 3 kilograms; the specific heat of food about 0.8 that of water. The absorption of body-heat therefore by the food amounts approximately to $3 \times 0.8 \times 25°\text{C.} = 60$ Calories $= 2.8$ per cent. With the removal of the end-products of the foods and drink from the body an equal amount of heat is carried out.
2. *In Warming the Inspired Air.*—The average temperature of the air is 12°C.; the amount of inspired air, about 15 kilograms; the specific heat of air, 0.26. The absorption of body-heat by the air until it attains the temperature of the body will therefore amount to $15 \times 0.26 \times 25° = 97.5$ Calories $= 3.8$ per cent. The expired air removes from the body a corresponding amount.
3. *In the Evaporation of Water from the Lungs.*—The quantity of water evaporated from the lungs may be estimated at 400 grams; as each gram requires for its evaporation 0.582 Calorie, the quantity of heat lost by this channel would be $400 \times 0.582 = 232.8$ Calories $= 9.4$ per cent.
4. *In the Evaporation of Water from the Skin.*—The quantity of water evaporated from the skin may be estimated at 660 grams, causing a loss of heat by this channel of $660 \times 0.582 = 384.1$ Calories $= 15.3$ per cent.
5. *In Radiation and Conduction from the Skin.*—The amount of heat lost by this process can be indirectly determined only by subtracting the total amount lost by the above-mentioned channels from the total amount produced. Thus, $2500 - 7774.4 = 1725.6$ Calories $= 69$ per cent. would represent the average amount lost by radiation and conduction.

The Mechanism of Heat-dissipation.—As stated in foregoing paragraphs heat-dissipation is accomplished mainly by radiation and conduction from the skin, 70 per cent., and by evaporation of water from the skin and lungs, 25 per cent. The heat dissipated in warming food, drink and air inspired, or what amounts to the same thing in raising the excretions, urinary, fecal and respiratory to the body-temperature, may be here neglected. The relative amounts dissipated by these two routes, radiation and evaporation of water, will depend largely on the external temperature in so far as it is not interfered with by clothing and artificial temperatures.

The mechanism by which the dissipation is accomplished consists of the cutaneous and respiratory blood-vessels and the sweat-glands, together with the heart and respiratory apparatus, which collectively therefore may be regarded as thermolytic organs, all of which are made to coöperate by the intermediation of the nerve system, especially the vaso-motor and secretory portions of it. With a given external temperature such as characterizes the spring months, there is a certain ratio between the percentage of heat lost by radiation and by water evaporation. As the temperature rises as it does during the summer months, the cutaneous vessels dilate as a result of a reflex inhibition of the vaso-motor center due to the stimulating action of the heat on the cutaneous nerve endings, which brings to the surface a larger volume of blood, a condition favorable to increased radiation. This, however, is to some extent prevented by reason of a diminution of the difference in temperature between that of the atmosphere and that of the body.

The sweat-glands at the same time are stimulated to increased activity, and in consequence of the additional volumes of blood brought to the skin a larger amount of sweat is secreted, which speedily undergoes evaporation. As each gram of water for its evaporation requires 0.582 of a calorie, it is evident that increased secretion of sweat favors heat-dissipation. The nerve-centers influencing the activity of the sweat-glands may be stimulated not only reflexly, but directly by an excess of heat in the blood. If, however, the atmosphere itself possesses a high percentage of moisture, evaporation from the body is much diminished and the value of sweating as a means of lowering the body-temperature is much impaired. Evaporation is hastened by air in motion. Hastened respiratory movements and the dilatation of blood-vessels of the respiratory surface also increase the evaporation of water from the lungs and thus occasion a greater loss of heat.

When the external temperature falls as, it does in the autumn and winter months, there is a decrease in the physiologic activity of the skin from a contraction of the blood-vessels, a diminution of the blood-supply, and a cessation in the secretion of sweat due to increased activity of the general vaso-motor center. The blood, being prevented from coming to the surface, is retained in the deeper portion of the body, and in consequence the conditions for radiation are diminished. Nevertheless by reason of the increase in the difference of temperature between that of the air and that of the body, radiation takes place to a greater extent than during the summer months. These variations in the cutaneous circulation in response to variations in the external temperature are brought about by the vaso-motor nerve mechanism; and as they take place with extreme promptness heat-dissipation and heat-production are quickly adjusted and the mean temperature maintained.

Radiation from the skin is modified to some extent by clothing. An excess of clothing diminishes, a diminution of clothing increases radiation. The quality of clothing is also an important factor. Wool is a poor conductor of heat but a good absorber and retainer of moisture, and hence is adapted for cold weather. Linen and cotton possess the opposite qualities, and hence are adapted for warm weather. Radiation from the skin is somewhat interfered with by subcutaneous fat, the extent of the interference being dependent on its amount.

Inasmuch as the mean temperature of the body remains practically constant, notwithstanding seasonal variations, it is apparent that heat-dissipation must be exactly balanced by heat-production. Should there be any want of correspondence between the two processes, there would arise either an increase or a decrease in the mean temperature. As both heat-production and heat-dissipation are variable factors, dependent on a variety of internal and external conditions, their adjustment is accomplished by a complex self-regulating mechanism involving muscle, vascular, and secretor elements, coördinated by the nerve system.

The Influence of the Nerve System.—Even though it is admitted that the heat liberated is the result of the metabolizing power of muscles and glands, and other tissues as well, and even though it is further admitted that the heat liberated is increased when the tissues (muscles) are excited to action under the stimulating influence of the efferent nerve system, nevertheless the question has been raised whether in addition, there are not special nerves and nerve-centers, the specific function of which is to stimulate metabolism at all times and thus provide for a continuous production of heat, the amount of which from day to day, varying with the extent of the losses. In this case the heat liberated by muscles at the time of their contraction would be incidental and not to be regarded as a necessary part of the fundamental heat-producing mechanism.

This view is apparently supported by the increase in heat-production that follows injuries or lesions of certain portions of the nerve system. Thus injury to the caudate nucleus or to the tuber cinereum, in an animal is promptly followed by a rise in the body-temperature of from four to about seven degrees; while lesions of the cortex of the animal in the neighborhood of the cruciate sulcus and at the junction of the supra-sylvian and post-sylvian fissures is promptly followed by a fall in the body-temperature. These and many other facts have led to the formation of a theory as to the manner in which heat-production is excited and regulated by the nerve system in accordance with variations in external temperature. In this theory it is assumed that, throughout the anterior horns of the gray matter of the spinal cord there are nerve-cells that give origin to nerve-fibers that pass out in the ventral roots of the spinal nerves, to be distributed in company with them to muscles at least, and excite heat-production even though the muscles are not in active contraction. These centers and nerves are termed, respectively, *thermogenic centers* and *thermogenic nerves.* The thermogenic centers it is further assumed, though continuously active, are not influenced directly by nerve impulses transmitted to them from the skin in consequence of changes in the external temperature nor by changes in the temperature of the blood, but are influenced by nerve impulses descending the nerve system from higher levels.

Experimental investigations have apparently demonstrated that an injury or stimulation of the caudate nucleus or of the tuber cinereum is very promptly followed by an increase in heat-production, which leads to the inference that there are in these regions groups of nerve-cells which when stimulated increase heat-production. To this group of cells the term *thermo-accelerator* has been given.

Experimental investigations have also apparently demonstrated the fact that injuries or stimulation of the cerebral cortex in the neighborhood of the cruciate sulcus and at the junction of the supra-sylvian and post-sylvian fissures (dog) is promptly followed by a decrease in heat-production which leads to the inference that there are in these regins groups of nerve-cells stimulation of which decreases heat-production. To this group of cells the term *thermo-inhibitor* has been given. Both these centers are in direct connection by nerve-fibers with the thermogenic centers in the spinal cord and through which they alternately accelerate or inhibit their activity.

The thermo-accelerator and thermo-inhibitor centers it is assumed are both connected with the cutaneous surface through the intermediation of afferent nerves and, therefore, in a position to be influenced by changes in the external temperature. Evidence is also at hand that they may be influenced by changes in the temperature of the blood passing to and around them. A fall of the external temperature develops nerve impulses which transmitted to the thermo-accelerator center excite it to action and thus increase heat-production; a rise in external temperature, on the other hand, has an opposite effect by stimulation of the inhibitor center.

The regulation and maintenance of the mean temperature or *thermotaxis* is, therefore, the result of an adjustment between heat-production and heat-dissipation, both of which are variable factors, and is accomplished by a complex, self-regulating mechanism consisting of muscle, vascular and secretor elements coördinated by the nerve system. Given this mechanism and the variations in the external temperature the metabolizing power of the living material is caused to vary in one direction or another as the external temperature rises and falls.

CHAPTER XVII

EXCRETION

Excretion may be defined as the process by which the end-products of tissue metabolism are removed from the body, the nature of the process, however, differing in no essential particulars from that underlying the process of secretion as stated in preceding chapters. The histologic structures involved and the forces at work being of the same general character, it is impossible to draw any sharp line of distinction between them. As a general fact it may be stated, that in their composition all the characteristic ingredients of the excretions are incapable either of entering into the formation of tissue or of undergoing oxidation for the purpose of heat-production. As the retention of these end-products in the body would exert a deleterious influence on normal metabolism, their prompt removal becomes essential to the maintenance of physiologic activity. The principal excretions of the body—urine, perspiration, and bile—are, with the exception of those given off in the lungs, complex fluids in which are to be found in varying proportions the chief end-products of metabolism.

THE URINE

The urine is a fluid formed by the activities of the kidneys and characterized by well-marked physical properties and a complex chemical composition. After its formation in the kidneys it passes through the ureters into the bladder, where it is temporarily retained before being discharged from the body.

Physical Properties.—Normal urine has a pale yellow or amber color, an aromatic odor, an acid reaction, and a specific gravity of 1.020. As a rule, it is perfectly transparent, though its transparency may be diminished from the presence of mucus, calcium and magnesium phosphates, and mixed urates.

The *color,* which varies within physiologic limits from a pale yellow to a reddish-brown, is due to the presence of the coloring-matters, *urochrome, urobilin,* and *uroerythrin,* all of which are derivatives of the bile pigments absorbed from the liver or the alimentary canal.

The *odor* of the urine is characteristic and due to the presence of volatile organic compounds.

The *reaction* of the urine is generally acid to litmus. The reaction has been for a long time attributed to the presence of sodium dihydrogen phosphate, though it is more probably due to the presence of various acid radicals. The intensity of the acidity will depend on the extent to which any particular acid is dissociated with the liberation of the hydrogen ions as it is the latter factor that imparts acidity to the fluid. The degree of acidity, however, varies at different periods of the day. Urine passed in the morning is strongly acid, while that passed during and after digestion, especially if the food be largely vegetable in character and rich in alkaline salts, is either neutral or alkaline in reaction. The diminished acidity after meals is attributed to the formation of hydrochloric acid by the gastric glands and the consequent liberation of bases which are excreted in the urine. The phosphoric acid which enters into combination with sodium and potassium bases is a product of tissue metabolism.

The *specific gravity* is about 1.020, though it varies from 1.015 to 1.025. It will diminish, other things being equal, with increased consumption of water and diminished activity of the skin; it will be increased of course by the opposite conditions.

The *quantity* of urine excreted in twenty-four hours varies from 1200 to 1700 c.c. Amounts both above and below these are frequently passed from a variety of causes.

Chemic Composition.—The chemic composition of the urine is very complex and is determined partly by the metabolism of the constituents of the tissues and partly by the quantity and the quality of the food consumed and metabolized. Hence the composition will vary from day to day in accordance with the character of the food. An average composition is presented in the following table:

THE CHEMIC COMPOSITION OF URINE

Water	1500.00 c.c.
Total solids	72.00 grams.
Urea	33.18 grams.
Uric acid (urates)	0.55 grams.
Hippuric acid (hippurates)	0.40 grams.
Kreatinin, xanthin, hypoxanthin, guanin, ammonium salts, pigment, etc	11.21 grams.
Inorganic salts; sodium and potassium sulphates, phosphates, and chlorids; magnesium and calcium phosphates	27.00 grams.
Organic salts: lactates, acetates, formates in small amounts	
Sugar a	trace
Gases, nitrogen, and carbonic acid.	

The Total Solids.—It is frequently a matter of clinic interest to determine the total amount of the solid constituents excreted in twenty-four hours. This may be attained approximately by multiplying the last two figures of the specific gravity by the coefficient 2.33 of Haeser or Christison. The coefficient of Jones, 2.6, is believed by some observers to give more accurate results for conditions existing in this country. The result expresses the total solids in 1000 parts: *e.g.*, urine with a specific gravity of 1.020 would contain 20 × 2.33, or 46.60 grams of solid matter per 1000 c.c. If the amount passed in twenty-four hours be 1500 c.c., the total solids would amount to 69.9 grams daily.

The Water of the Urine.—The amount of urinary water and its ratio to the solid constituents will vary with the amount consumed and the activity of the skin and lungs. In summer the foods, liquid and solid, remaining the same, the quantity of water in the urine is diminished in consequence of increased activity of skin and lungs and the ratio of water to solids decreased. In winter the reverse conditions obtain. The food remaining the same, the consumption of large quantities of water hastens at least the removal of end-products from the tissues and thus increases the urinary solids.

Urea.—Urea is the most abundant of the organic constituents of the urine and is present to the extent of from 2 to 3 per cent. It is a colorless neutral substance, crystallizing under varying conditions in long silky needles or in rhombic prisms. It is soluble in water and alcohol. It is composed of CON_2H_4. When subjected to prolonged boiling, it combines with water, giving rise to ammonium carbonate. The presence of *Micrococcus ureæ* in urine will also convert the urea, by combining it with two molecules of water, into ammonium carbonate, $CON_2H_4 + 2H_2O = (NH_4)_2CO_3$.

The amount of urea excreted each day varies from 30 to 40 grams, the average being about 34 grams and therefore represents an amount of protein metabolized equivalent to from 90 to 120 grams or an average of about 100 grams. The remaining nitrogen-holding compounds in the urine represent as shown by their nitrogen content a protein metabolism of about 12 grams. As to how much of the urea or of the total nitrogen is derived from the metabolism of tissue protein and how much from the metabolism of the food protein that is not elaborated into tissue protein, is difficult to state. It has been observed however in human beings in the fasting condition that for a period of 10 days, there is a daily excretion of about 21 grams of urea equivalent to about 63 grams of protein metabolized. If it be accepted that approximately 63 grams of tissue protein are metabolized each day then of the 34 grams of urea excreted, 13 grams must come from about 40 grams of metabolized food protein. That the urea that comes from the tissue protein is a rather constant factor and that the urea that comes from the food protein is a variable factor is shown by the fact that the amount of urea excreted rises and falls proportionately to the protein consumed. As to the particular tissues that are undergoing protein metabolism there is much obscurity. Contrary to what might be expected there is apparently but little protein metabolism in muscle tissue for there is no parallel ism between urea production and muscle work. Even after severe labor extending over a period of some hours there is no noticeable increase in the urea excreted.

Seat of Formation and Antecedents of Urea.—It has been stated in a foregoing paragraph that the excretory organs are engaged in the process of eliminating from the blood, rather than in elaborating, the end-products of metabolism. Therefore the supposition is that the kidneys are not the seat of urea formation but only the means by which it is eliminated from the blood. This supposition is rendered highly probable from the following facts: the blood of the renal artery contains from one-third to one-half more urea than the blood of the renal vein; ligation of the renal arteries or removal of the kidneys leads to an accumulation of urea in the blood to an extent four times the normal amount in 24 hours; perfusion of the excised kidney, which still retains its physiologic activity, with blood containing known antecedents of urea is unattended with urea formation. These and other facts of a similar character confirm the view that the kidney does not manufacture but simply excretes urea brought to it by the blood. Since urea is always present in the blood to an extent of from 0.04 per cent. to 0.06 per cent., *i.e.*, from 4 to 6 grams per 10,000 grams, and that it is being excreted at the rate of about 1.5 grams per hour, it is evident that it is being as constantly formed in some one or more organs, and discharged into the blood.

The experimental evidence now at hand indicates the liver as the chief organ engaged in this process. The following facts support this view, viz.: destructive diseases of the liver, *e.g.*, acute yellow atrophy, interstitial hepatitis, and suppuration, largely diminish the production of urea but increase the amount of the ammonium salts in the urine; the establishment of an Eck fistula (the union of the portal vein with the ascending vena cava whereby the liver is almost entirely excluded from receiving compounds absorbed from the intestine) is followed by a decrease in the production of urea and an increase in the ammonium content of the urine; the perfusion of the liver of a recently killed animal with a given amount of blood containing ammonium salts will be followed after the lapse of several hours by an amount of urea in the blood two or three times the normal quantity. These and other facts indicate that the chief seat of urea formation is to be found in the liver cells.

The antecedents of urea, out of which the hepatic cells construct urea have, for chemic reasons as well as from the foregoing experimental results, been shown to be the salts of ammonia the carbonate, carbamate, and lactate. The increase in the ammonia of the urine simultaneously with the decrease in the urea renders it extremely probable that these salts are antecedents of urea and that the transformation takes place in the liver cells. The chemic change that takes place is simply the abstraction of two molecules of water as shown in the following formula:

$$(NH_4)_2CO_3 - 2H_2O = CON_2H_4.$$

The source of the ammonia is probably in part the intestine, as this compound is one of the products of the hydrolysis and cleavage of the proteins during digestion. That this is the case is apparent from the fact that the blood of the portal vein always contains more ammonia that the blood of any other region of the vascular apparatus. The advantage to the body that results from the conversion of ammonia to urea is that it prevents an ammonia intoxication with its attendant evils that would otherwise arise.

It will be remembered that the amino-acids, as tyrosin, leucin, glutamic, and aspartic acids, diamino-acids and bases, as lysin, arginin, histidin which are also products of the hydrolysis of proteins during digestion are capable of being absorbed as such by the epithelial cells of the villi and mucous membrane. After absorption they are transmitted by the blood to the tissues of the body generally by which they are directly utilized in the formation of tissue protein or perhaps stored for future use, for there is evidence for the belief that tissues have a capacity for the storage of amino-acids, which in the case of muscles amounts to from 70 to 80 milligrams per 100 grams. After saturation of the tissues, so to speak, with amino-acids, there yet remains a certain percentage in the blood which undergoes a cleavage into an NH_2 portion and an organic portion; the former is then converted to ammonia and subsequently to urea by the liver cells, the latter, the organic portion, contributes to the production of fat or sugar, which in due time is oxidized and thus contributes to the store of body-heat.

From the foregoing facts it is evident that given the presence of ammonia salts in the blood of the portal vein the appearance of urea in the urine is readily accounted for. There is also evidence for the belief that in the muscles and perhaps other tissues as well, amino-acids, those resulting from the metabolism of tissue protein, as well as those stored, undergo a similar chemic change with the formation of urea. This being the case, the muscles must be regarded as a seat of urea formation.

Uric Acid.—Uric acid is one of the constant ingredients of the urine. It is a crystalline nitrogen-holding body closely resembling urea, its formula being $C_5H_4N_4O_3$. The total quantity excreted daily varies from 0.2 to 1 gram. It is doubtful if uric acid exists in a free state in the urine, the indications being that it is combined with sodium and potassium in the form of a quadriurate. The urates when in excess are frequently deposited from the urine as a brick-red sediment, the color being due to their combination with the coloring-matter uroerythrin. When pure, uric acid crystallizes in the rhombic form, though it assumes a variety of forms. Uric acid was long regarded as a product of general protein metabolism. This view has been abandoned. At present it is believed that it is a cleavage product of nuclein, a constituent of all cell nuclei. In the metabolism of nuclein a protein and nucleic acid are formed, from the latter of which uric acid is derived. Nucleic acid when decomposed yields bases, such as guanin, adenin, etc., which under the action of the enzymes *guanase* and *adenase* are combined with water, deaminized, and converted into xanthin and hypoxanthin. Because of the fact that these bodies can also be obtained from a synthesized body termed *purin* they are known collectively as the purin bases. Though there is a close relationship between uric acid and the purin bases, it has been impossible experimentally to derive one from the other. When hypoxanthin, however, is given internally it is oxidized and converted into uric acid. It is extremely probable, therefore, that uric acid is an oxidation product of one or more of the purin bases.

It is probable, however, that not all of the uric acid eliminated is derived from the nuclein of tissue cells and their decomposition products, the purin bases. Some of it is undoubtedly derived from the nucleins contained in foods. The uric acid eliminated is therefore partly endogenous and partly exogenous in origin.

There is some evidence that not all the uric acid produced in the body is excreted as such, but, that a portion, perhaps one-half, is changed to urea.

Adenin, Guanin, Xanthin, Hypoxanthin.—These compounds are also found in urine in small but variable amounts. They are nitrogenized compounds derived mainly from the metabolism of the nuclein bodies.

Kreatinin.—This is a crystalline nitrogenous compound closely resembling kreatin, one of the constituents of muscle-tissue. The amount excreted daily is about 1 gram. The origin of kreatinin is not very clear. It is probable, however, that if kreatin is capable of transformation into kreatinin a certain portion is derived from the kreatin contained in the meat consumed as food. But as kreatinin is steadily excreted though in less amounts on a diet from which meat is excluded it is certain that this portion at least must have some other source containing nitrogen, and the inference is that it is one of the end-products of the protein metabolism that is taking places in tissues generally and more particularly in muscle-tissue.

Hippuric Acid.—This acid in combination with sodium and potassium is very generally present in urine, though in small amounts. It is more abundant in the urine of the herbivora than the carnivora. In man the amount excreted daily is about 0.7 gram, though the amount may be raised by a diet of asparagus, plums, cranberries, etc., and by the administration of benzoic and cinnamic acids. There is evidence that hippuric acid is formed in the kidney from benzoic acid, its precursors, or related bodies. Various compounds of this class are found in vegetable foods, a fact which may account for the increase in the excretion of hippuric acid on a vegetable diet.

Indol, Skatol, Phenol, Cresol.—These compounds, products of the putrefactive changes in the derivatives of protein are present in variable amounts, associated with potassium sulphate (see page 205). These compounds are known as the ethereal sulphates. The extent to which they are present is taken as a measure of the extent of intestinal putrefaction; their presence can be determined by various tests. Of these compounds the one generally tested for is potassium indoxyl sulphate or *indican*. If hydrochloric acid and a small quantity of sodium hypochlorite be added to suspected urine, together with a few cubic centimeters of chloroform, the indican if present will be separated by the acid into indoxyl and potassium sulphate. The former compound will then be oxidized by the oxygen set free from the sodium hypochlorite and form *indigo blue*. The chloroform will absorb the indigo blue as fast as formed and when the reaction is completed will accumulate at the bottom of the test-tube. The depth of the color is indicative of the quantity present and of the extent of the intestinal putrefaction.

Inorganic Salts.—Sodium and potassium phosphates, known as the *alkaline phosphates*, are found in both blood and urine. The total quantity excreted daily is about 4 grams. Calcium and magnesium phosphates, known as the *earthy phosphates*, are present to the extent of 1 gram. Though insoluble in water, they are held in solution in the urine by its acid constituents. If the urine be rendered alkaline, they are at once precipitated. Sodium and potassium sulphates are also present to the extent of about 2 grams. The phosphoric and sulphuric acids which are combined with these bases enter the body for the most part in the foods, though there is evidence that they also arise by oxidation in consequence of the metabolism of proteins which contain phosphorus and sulphur. Sodium chlorid is the most abundant of the inorganic salts. It is derived mainly from the food. The amount excreted is about 15 grams in twenty-four hours.

THE KIDNEYS

The **kidneys** are the organs engaged in the excretion of the urinary constituents from the blood. Each kidney resembles a bean in shape, is from 10 to 12 centimeters in length, 2 centimeters in breath, and weighs from 144 to 170 grams. These organs are situated in the lumbar region, one on each side of the vertebral column behind the peritoneum, and extend from the eleventh rib to the crest of the ilium. The anterior surface is convex, the posterior surface concave. The latter presents a deep notch—the hilum. The kidney is surrounded by a thin smooth membrane composed of white fibrous and yellow elastic tissue; though it is attached to the surface of the kidney by minute processes of connective tissue, it can very readily be torn away. The substance of the kidney is dense but friable.

Upon making a longitudinal section of the kidney it will be observed that the hilum extends into the interior of the organ and expands to form a cavity known as the sinus, in which are found the blood-vessels, nerves, and duct (Fig. 205). This cavity is mainly occupied by the upper part of the renal duct, the ureter, the interior of which is termed the pelvis. The ureter divides into several portions which terminate in small caps or calyces which receive the apices of the pyramids. The parenchyma of the kidney consists of two portions, viz.:

1. *An internal* or *medullary portion*, consisting of a series of pyramids or cones, some twelve or fifteen in number, which present a distinctly striated appearance.

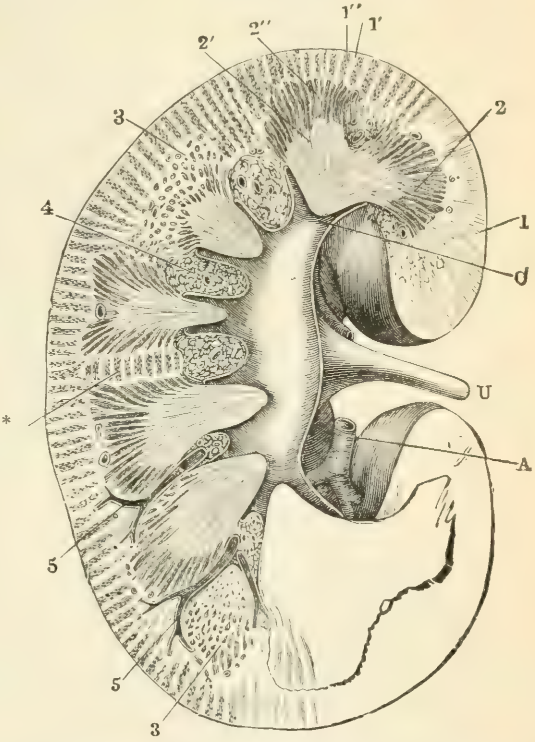

FIG. 205.—LONGITUDINAL SECTION THROUGH THE KIDNEY, THE PELVIS OF THE KIDNEY, AND A NUMBER OF RENAL CALYCES. A. Branch of the renal artery. U. Ureter. C. Renal calyx. 1. Cortex. 1′. Medullary rays. 1″. Labyrinth, or cortex proper. 2. Medulla. 2′. Papillary portion of medulla, or medulla proper. 2″. Border layer of the medulla. 3, 3. Transverse section through the axes of the tubules of the border layer. 4. Fat of the renal sinus. 5, 5. Arterial branches. *. Transversely coursing medulla rays.—(*Tyson, after Henle.*)

2. *An external* or *cortical portion*, half an inch in thickness and distinctly friable in character.

A histologic analysis of the kidney shows that it is composed of a connective-tissue framework supporting secreting tubules, blood-vessels, lymphatics and nerves, all of which are directly connected with the removal of the urinary constituents from the blood.

The Tubules of the Kidney.—From its structure it is apparent that the kidney is a compound tubular gland, the orifices of exit being directed toward the pelvis. If the apex of each pyramid be examined with a lens, it will present a number of small orifices which may be regarded as the beginnings of the uriniferous tubules. From this point the tubules pass outward in a straight but somewhat diverging manner toward the cortex, giving off at acute angles a number of branches (Fig. 206). From the apex to the base of the pyramids they are known as the tubules of Bellini. In the cortical portion of the kidney the tubule becomes enlarged and twisted, and, after pursuing an extremely convoluted course, turns backward into the medullary portion for some distance, forming the ascending limb of Henle's loop; it then turns upon itself, forming the descending limb of the loop, reënters the cortex, again expands and becomes convoluted, and finally terminates in an ovoid invaginated enlargement known as Müller's or Bowman's capsule, which receives a small tuft of blood-vessels—the *glomerulus*. Each tubule consists of a basement membrane lined throughout its entire extent by epithelial cells. The epithelium as well as the tubule varies in shape and size in different parts of its course. In the capsule the epithelium is flattened, lining not only the inner surface of the capsule but reflected over the blood-vessels as well. This is known as the glomerular epithelium. In the convoluted portions of the tubules the epithelium is cuboid, granular, and somewhat striated; in Henle's loop it is more or less flattened.

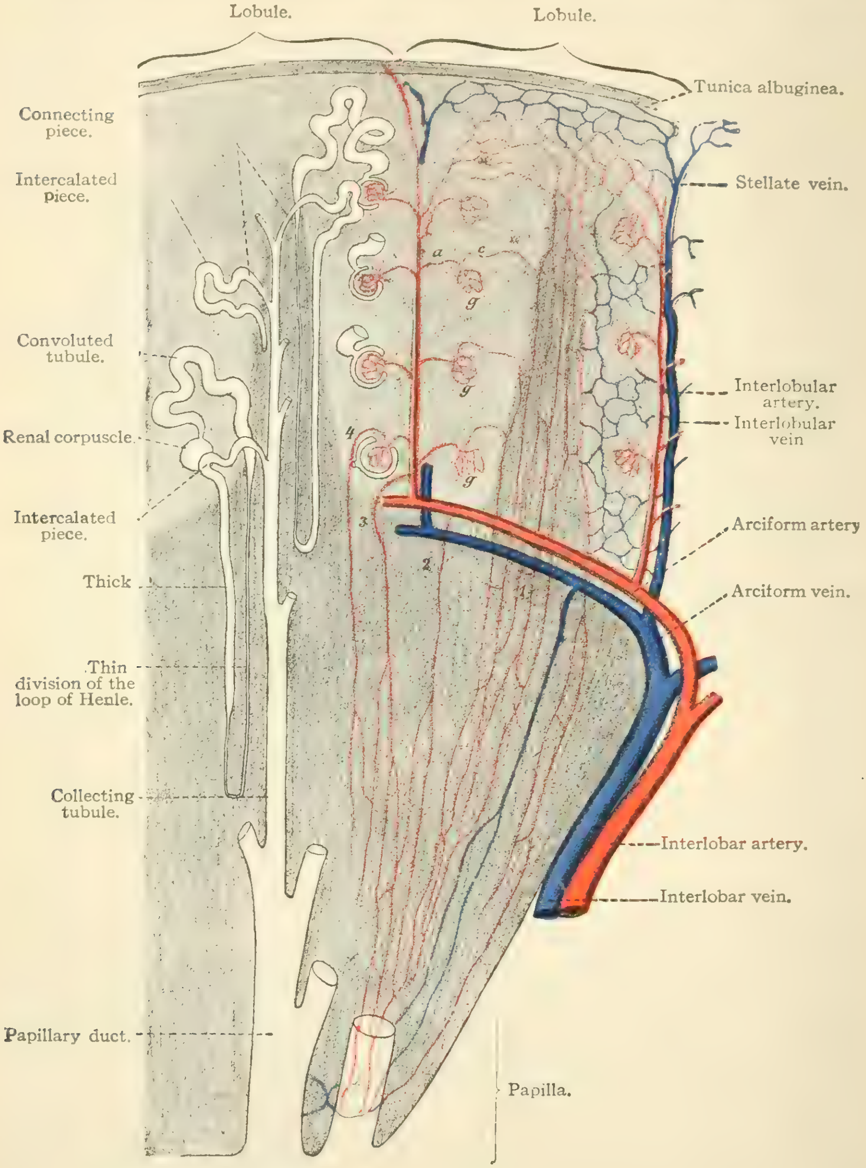
Lobule.
Lobule.
Tunica albuginea.
Connecting piece.
Intercalated piece.
Stellate vein.
a
c
g
g
g
Convoluted tubule.
Interlobular artery.
Interlobular vein
4
Renal corpuscle.
3
2
1
Intercalated piece.
Arciform artery
Arciform vein.
Thick
Thin division of the loop of Henle.
Collecting tubule.
Interlobar artery.
Interlobar vein.
Papillary duct.
Papilla.

FIG. 206.—SCHEME OF THE COURSE OF THE URINIFEROUS TUBULES AND THE RENAL VESSELS. (*Stöhr.*)

The Blood-vessels of the Kidney.—The renal artery enters the kidney at the hilum behind the ureter; it soon divides into several large branches which penetrate the substance of the kidney between the pyramids and pass outward into the cortex. At the base of the pyramids branches of the arteries form an anastomosing plexus. From this plexus vessels are given off, some of which follow the straight tubules toward the apex of the pyramids, vasa recta, while others enter the cortex and pass to its surface (Fig. 218). In the course of the latter, small branches are given off, each of which soon divides and subdivides to form a ball of capillary vessels known as the *glomerulus.* These capillaries, however, do not anastomose, but soon reunite to form an efferent vessel the caliber of which is less than that of the afferent artery. In consequence of this, there is a greater resistance to the outflow of blood than to the inflow, and therefore a higher blood-pressure in the glomerulus than in capillaries generally. The relation of the glomerulus to the tubule is important from a physiologic point of view. As stated above, the glomerulus is received into and surrounded by the terminal expansion or capsule of the tubule. This capsule, formed by an invagination of the terminal portion of the tubule, consists of two walls, an outer one consisting of an extremely thin basement membrane, covered by flattened epithelial cells, and an inner one consisting apparently only of flattened epithelium which is reflected over and closely invests the glomerular blood-vessels (Fig. 207). The blood is thus separated from the interior of the capsule by the epithelial wall of the capillary and the epithelium of the reflected wall of the capsule. During the periods of secretor activity the blood-vessels of the glomerulus are filled with blood to such an extent that the sac cavity is almost obliterated. After its exit from the capsule the efferent vessel of the glomerulus soon again divides and subdivides to form an elaborate capillary plexus which surrounds and closely invests the convoluted tubules. From this plexus as well as from the plexus which surrounds the straight tubules veins arise which pass toward and empty into the interlobular veins as well as the veins at the base of the pyramids. The renal veins formed by the union of these latter veins emerges from the kidney at the hilum and finally empties into the vena cava inferior.

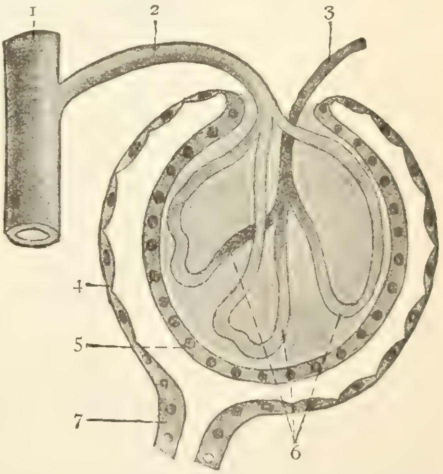

Fig. 207.—Scheme of the Renal or Malpighian Corpuscle. 1. Interlobular artery. 2. Afferent vessel. 3. Efferent vessel. 4. Outer wall. 5. Inner wall. 6. Glomerulus. 7. Neck of tubule.—(*Stöhr.*)

The Nerves of the Kidney.—The nerves distributed to, and associated with the functional activities of the kidney consist of both pre- and post-ganglionic fibers. The latter have their origin in the cells of small ganglia situated close to the semilunar ganglion. From their origin they pass through the renal plexus and follow the course of the blood-vessels to their termination. The former, the preganglionic nerves, have their origin in the lower portion of the thoracic region of the spinal cord and pass forward in the small splanchnic nerves. Experiment has shown that these nerve-fibers have both vaso-constrictor and vaso-dilatator functions. The presence of specific secretor fibers for the epithelium has not been satisfactorily demonstrated.

The Renal Duct.—The renal duct, the ureter, is a musculo-membranous tube about 5 mm. in diameter when distended, 30 cm. in length, and extends from the hilum to the base of the bladder into which it empties. The upper extremity is expanded and within the renal sinus becomes irregularly branched, giving rise to a number of short tubes, called calyces, each of which embraces the apex of a Malpighian pyramid. The interior of the expanded portion of the ureter is known as the *pelvis*. The wall of the ureter consists of a mucous membrane, a muscle coat, and an external fibrous investment.

MECHANISM OF URINE SECRETION

The physiologic mechanism concerned in the secretion of the urine, reduced to its simplest terms, consists of (1) the afferent vessel, the glomerulus, the efferent vessel, the capillaries and the veins; (2) the glomerular capsule and the epithelium of the tubule throughout its entire extent. Fig. 208.

The secretion of urine by this mechanism is a complex process and susceptible of several interpretations. It was originally inferred by Bowman, an inference based on the histologic structure of the blood-vessels and tubules and their relation one to the other, that there is here present (1) an apparatus for filtration, the capsule with its enclosed glomerulus, and (2) an apparatus for secretion, the tubule with its epithelium, and therefore the elimination of the urinary constituents from the blood is accomplished by the two processes of filtration and secretion; that the water and highly diffusible inorganic salts simply pass by filtration, under pressure, through the walls of the glomerular capillaries, while the organic constituents are removed by the epithelium lining the tubules; that the water, descending the tubules from the capsules, plays the part of a solvent for the crystallizable compounds secreted by the epithelium, in consequence of which they are the more readily carried by the moving fluid into the pelvis of the kidney.

Ludwig, influenced largely by the facts of blood-pressure, advanced the view a few years later that the factors concerned in the secretion of urine are purely physical; that in consequence of the high pressure in the vessels of the glomeruli, due to the high pressure in the renal artery on the one hand, and to the resistance offered by the smaller efferent vessel on the other hand, all the urinary constituents are filtered off in a state of extreme dilution. In order to account for the higher percentage of the organic constituents in the urine than in the blood, it was assumed that as the dilute urine passed through the tubules the water and possibly other substances as well, that were necessary for the nutrition of the body, were partly reabsorbed, passing by diffusion into the lymph and blood until the urine acquired its normal characteristics and degree of concentration. In support of this view, a large number of facts relating to the influence of an increase and a decrease of pressure in the blood-vessels of the glomeruli, the velocity of the blood-stream, etc., in determining the rate of urinary flow were adduced, all of which apparently indicated that the former stood to the latter in the relation of cause and effect, and that the formation of urine was accomplished entirely by purely physical forces.

The progress of physiologic investigation, however, has thrown some doubt on the validity of this physical interpretation.

Heidenhain brought forward a series of facts which supported the view, that all the constituents of the urine are eliminated from the blood by a process of secretion on the part of the epithelial cells both of the glomerulus and the tubules; that these cells have the power of selection in removing from the blood normal diffusible constituents when in excess, and abnormal constituents, *i.e.*, urea, uric acid, etc., when present in any amount, recognizing at the same time that the secretor activity of these cells is modified in one direction or another by the blood-pressure and the variations which it undergoes from moment to moment. In other words that the secretion of urine is a physiologic or vital process, rather than a physical or mechanical process. As evidence that the cells of the tubules possess a selective power, he presented the following experiment: The spinal cord of an animal is divided in the neck for the purpose of lowering the blood-pressure in the kidney below the pressure at which the urine is secreted. Five to twenty c.c. of a saturated solution of indigo-carmine are injected into the blood-vessels; after intervals varying from ten minutes to one hour the animal is killed, the blood-vessles washed out with alcohol for the purpose of precipitating the indigo-carmine *in situ*. Section of the kidney shows a uniform blue stain of the cortex alone (Fig. 209). Microscopic examination reveals the fact that the blue stain is due to the deposition of the pigment in the lumen and in the lumen border of the cells of the convoluted tubules (Fig. 210) and

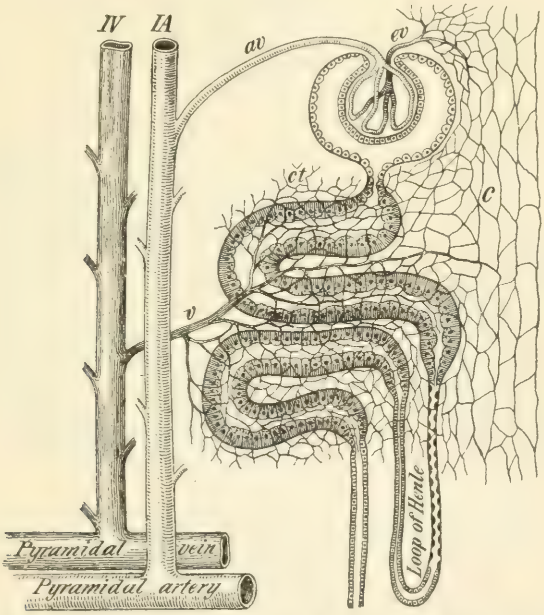

Fig. 208.—The Mechanism for the Secretion of the Urine. *I.A*, interlobular artery; *av*, afferent vessel; *ev*, efferent vessel; *c*, capillary vessels; *v*, vein; *IV*, interlobular vein; *ct*, contorted tubule.

the ascending limb of Henle's loop; while the epithelium of Bowman's capsule as well as the glomerular epithelium present no evidence of pigmentation. The physiologic action of the cells of the convoluted tubules in elimination of indigo-carmine, is supposed to indicate their action in the elimination of urea and other nitrogen-holding compounds. The absence of the pigment from the glomerular epithelium lends support to the view, that its function is the elimination of water and highly diffusible inorganic salts.

Another experiment which apparently shows the action of the epithelium is the following: A solution of uric acid in piperazin is injected into the blood of a rabbit. At the end of from twenty to sixty minutes the animal is killed. The kidney is sectioned and examined microscopically, whereupon it is found that crystals of uric acid are present in the epithelial cells of the contorted tubules, especially toward their inner border, while in the medullary tubules the crystals are confined to the lumen. These facts lead to the inference that under these conditions at least, the uric acid passes from the blood by way of the epithelium into the interior of the tubule to befinally discharged into the pelvis of the kidney.

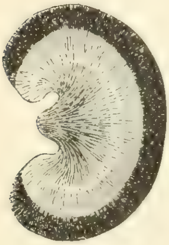

Fig. 209.—Kidney of a Rabbit. Cortex alone stained with the indigo-carmine at the end of one hour.—(*Heidenhain.*)

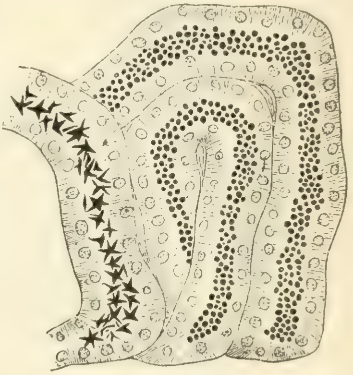

Fig. 210.—Microscopic Appearance of the Lumen of the Convoluted Tubules Containing the Indigo-carmine.—(*Heidenhain.*)

Nussbaum attempted to establish the secretory power of the epithelium in another way. In the frog the kidney receives blood from two sources: the glomeruli receive their blood from the renal artery, the tubules from the capillaries formed by the anastomosis of branches of the efferent vessel of the glomerulus and the branches of the renal portal vein. Nussbaum believed that by ligating the renal artery all glomerular activity could be abolished and the part played by the epithelium could be determined. After so doing the flow of urine was at once checked; the injection of urea at once reëstablished it. This fact was taken as a proof that the tubular epithelium not only excreted urea, but water and perhaps other constituents as well. It was also found that sugar, peptones, carmine, etc., which are always eliminated from the blood under normal conditions, are not removed after ligation of the renal artery. It was concluded from these experiments that the secreting structures of the kidney consist of two distinct systems, the glomerular and the tubular; the former secreting water, salts, sugar, peptone, etc., the latter urea, uric acid, etc. These and similar facts indicate that the renal epithelium possesses a secretor function. Heidenhain and those who agree with him assert that even the water and inorganic salts which pass through the glomerular epithelium do so in consequence of cell selection and cell activity; that the entire process is one of secretion, though conditioned by blood-pressure, blood velocity, etc.

The Present View as to the Mode of Formation of the Urine.— The still further progress of physiologic investigation has apparently reëstablished the view, subject to some modifications, that the glomerulus is after all but a passive apparatus permitting the filtration of water and diffusible salts, as Bowman and Ludwig suggested, and has confirmed the view of Heidenhain that the epithelium is a secretory apparatus, and in addition has established the further fact that the epithelium is an absorptive apparatus as well. Without presenting the details of a long series of experiments it suffices to say that the results of these investigations make it reasonably certain that the glomerulus permits of the passage of a filtrate, not of the character and composition asserted by Ludwig, but having the characteristics and composition of the blood-plasma, *i.e.*, having the chemic composition and the same degree of concentration as this fluid, less its protein content; that as this fluid passes through the tubules it receives the organic constituents which are secreted by the epithelium and in addition a certain volume of water as well; also that it loses water and inorganic salts which are returned to the blood not by diffusion as Ludwig believed but by an act of absorption on the part of the epithelial cells, when these substances are needed for nutritive purposes.

The probability that the renal epithelium possesses absorptive functions is indicated by a greater or less constriction of the tubules in those animals in which the retention of water at least, is desirable. Thus in fish, where the supply of water is abundant and no need for its retention in the body exists, the tubules are short, wide and free from any narrowing which would retard the downward flow of the fluid; in frogs which live partly on land and which lose water readily by evaporation from the skin, the retention of water is necessary, hence in these animals the tubules are long and much constricted; in tortoises where there is no evaporation from the skin, the tubes are short, wide and devoid of constrictions. In mammals the constricted portion, the loop of Henle, is long and narrow, and very probably serves to retard the flow of the liquid thus permitting of the absorption of water and other constituents.

Summarizing the foregoing it may be stated that the formation of urine is accomplished by the coöperation of the glomerulus and the epithelium of the renal tubules.

The *glomerulus* permits the passage of a filtrate similar if not identical with the blood plasma—minus the protein.

The *epithelium*, especially that lining the contorted portion of the tubule, (1) *secretes* water, various salts previously in combination with protein, *e.g.*, phosphates, urea, uric acid, various other nitrogen-holding compounds and organic matters; (2) *absorbs* such constituents of the urinary fluid as water and inorganic salts which may be necessary to the nutrition of the body. The final result of the entire process is the maintenance of the normal composition of the blood and body fluids.

The Influence of Blood-pressure.—Whether the elimination of the urinary constituents is entirely secretor (physiologic) in character or not there can be no doubt that the whole process is largely determined by the pressure and velocity of the blood in the glomerular capillaries, or, to state it more accurately, on the difference of pressure between the blood in the capillaries and the urine in the capsules. As a rule, this latter pressure is at a minimum. If the urine should accumulate in the ureter and tubules either from ligation or mechanical obstruction until its pressure approximated that of the blood, the secretion should be diminished if not abolished. It is difficult to determine the average pressure or velocity of the blood in the glomerular capillaries, though they both must be greater than in capillaries in other parts of the body, from the fact that the efferent vessel is narrower than the afferent, and therefore offers great resistance to the outflow of blood, a condition most favorable to the production of a high pressure in the glomerulus.

Glomerular Pressure.—The pressure of the blood in the glomeruli is the resultant of the pressure in the renal artery and the resistance to the outflow of blood through the efferent vessel and the capillaries beyond.

The pressure of blood in the renal artery may be augmented and the velocity of the blood stream increased:

1. By an increase in blood-pressure generally.
2. By an increase in the blood-pressure of the renal artery alone.

The first condition may be caused by an increase in either the force or frequency of the heart's action or by a contraction of the arterioles of the vascular areas in any or all parts of the body, excepting, of course, the renal vascular area. Should this condition arise, the blood would be forced into the renal artery in larger volumes and in consequence its pressure would be increased. The second condition is brought about by a dilatation of the renal artery alone and possibly by a simultaneous contraction of the efferent vessels of the glomeruli.

The pressure of the blood in the renal artery and therefore in the glomeruli may be diminished and the velocity decreased:

1. By a decrease in the blood-pressure generally.
2. By a decrease in the blood-pressure of the renal artery alone.

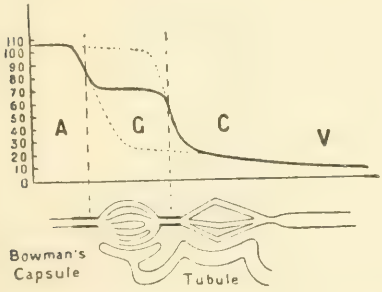

Fig. 211.—To Illustrate the Effect of Active Changes in the Vasa Afferentia and Efferentia on the Pressure in the Glomerular Capillaries. A. Renal arteries. G. Glomerular capillaries. C. Tubular capillaries. V. Vein. The short thick lines represent the vasa afferentia and efferentia. The continuous heavy line represents the mean average pressure. If the vas afferens dilates and the vas efferens contracts separately or conjointly, the pressure will rise, as indicated by the upper dotted line. If the vas afferens contracts and the vas efferens dilates separately or conjointly, the pressure will fall, as indicated by the lower dotted line.—(*After Morat.*)

The first condition may be caused by a decrease in either the force or frequency of the heart's action or by a dilatation of the arterioles of large vascular areas in any or all parts of the body. Should this condition arise, the volume of blood delivered to the kidney in the unit of time would be diminished and hence its pressure would fall. The dilatation of the cutaneous vessels in summer, the result of the high temperature leads to a diminished blood-supply to the kidney and a diminution in the amount of urine secreted. The second condition is brought about by contraction of the renal artery alone and possibly by a simultaneous dilatation of the efferent vessels of the glomeruli. Moreover the pressure in the vessels of the glomeruli may be varied according to the degree of contraction or relaxation of the muscle coat of the afferent and efferent vessels. See Fig. 211 and the accompanying explanation.

Coincident with the rise and fall of pressure in the glomerular capillaries there is a rise and fall in the rate of urinary flow. Thus it has been found that an increase in the aortic pressure from 127 to 142 mm. of mercury, from ligation of the carotid, femoral, and vertebral arteries, increased the rate of urinary flow from 8.7 grams in thirty minutes to 21.2 grams. On the contrary, a decrease in aortic pressure below 40 mm. of mercury caused by division of the spinal cord is followed by a total abolition of the urinary flow. These facts serve to indicate the dependence of the secretion on blood-pressure.

The period of functional activity of the kidney is accompanied by an increase in the volume of blood flowing through it as is evident from an inspection of the organ. At this time it is enlarged, swollen, and red in color. The blood in the renal vein is bright red in color and contains more oxygen and less carbon dioxid than venous blood generally. During the intervals of activity the kidney is supplied with a less amount of blood and hence it diminishes in size, becomes pale in color and the blood of the renal vein becomes dark and venous in character. These variations in the volume of the kidney have also been experimentally determined and registered by means of the oncometer and oncograph devised by Roy.

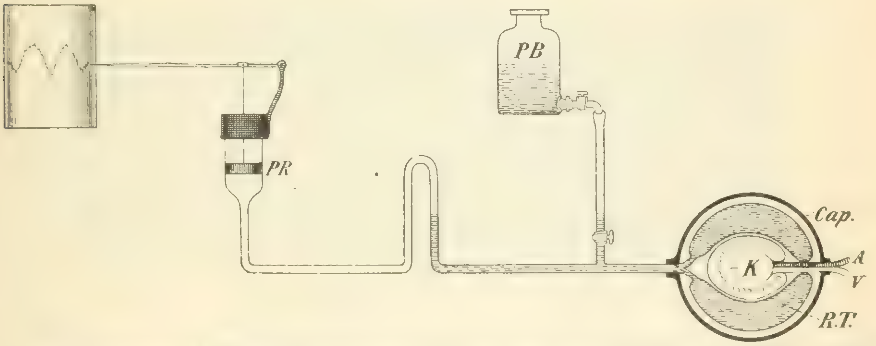

Fig. 212.—Scheme of a Renal Oncometer or Plethysmograph. *K*, kidney; *RT*, receiving tambour or capsule; *PB*, pressure bottle; *PR*, recording piston.

The Renal Oncometer.—The oncometer consists of a metallic capsule, (Fig. 212) composed of halves which open and close by means of a hinge. The capsule encloses two thin membranous and distensible sacs. These are connected with a piston recorder by means of a tube. The kidney, withdrawn from the body, is placed within the oncometer. Through an opening in the side pass the artery, vein, and ureter. A thin light oil is then poured through a side tube from a pressure bottle until the membranous sacs are completely filled and surround the kidney on all sides. When the tube from the pressure bottle is closed, the conditions are such that all variations in the volume of the kidney are taken up and reproduced by the lever attached to the piston recorder. A curve of the variations in the volume of the kidney is shown in Fig. 213. An examination of this curve shows that the volume-changes exhibit not only the respiratory but also the cardiac undulations.

The Influence of the Nerve System.—The influence of the nerve system in regulating the blood-supply to the kidney is evident from the results of experimentation. If the nerves which accompany the renal artery into the kidney are divided, the artery at once dilates, the kidney enlarges, and a copious flow of urine takes place. If the peripheral ends of these nerves be stimulated with induced electric currents the artery contracts, the kidney diminishes in size, and the flow of urine ceases. In addition to these vaso-constrictor nerves, there is evidence that the kidney also receives vaso-dilatator nerves. The vaso-constrictor nerves emerge from the spinal cord and are found in the anterior roots of the eleventh, twelfth, and thirteenth dorsal nerves, in the dog. Direct and reflex stimulation of the centers of origin of these nerves gives rise to contraction or to a dilatation of the artery, a diminution or a swelling of the kidney, and a decrease or an increase in secretion, independent of any variation in general blood-pressure according to the nature of the cause acting.

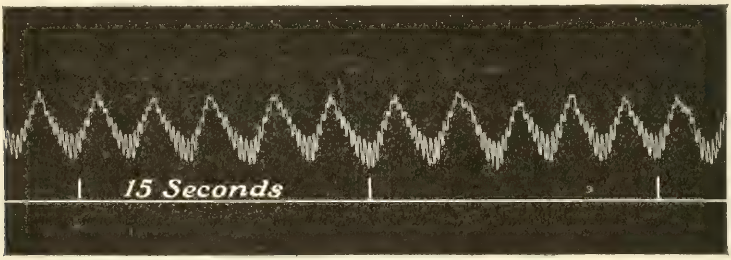

FIG. 213.—CURVE OF THE VARIATIONS IN THE VOLUME OF THE KIDNEY.

The route of the vaso-constrictor nerves is, in the dog at least, through the lesser splanchnics, the terminal branches of which arborize around the cells of the renal ganglia; from these ganglia new fibers arise which pass through the renal plexus into the kidney to be distributed to the muscle coat of the renal artery branches. Section of these nerves is followed by a dilatation of the renal vessels and an increase in the flow of urine. Stimulation of the peripheral ends is followed by a constriction of the vessels and a cessation of the flow of urine.

The vaso-motor center for the blood-vessels of the kidney is in all probability situated in the medulla oblongata in close proximity to the general vaso-motor centers, though subordinate centers are doubtless present in the spinal cord. It was found by Bernard that puncture of the medulla was occasionally followed by a profuse secretion of urine without the presence of sugar. The route of the vaso-motor impulses which influence the renal blood-supply is down the cord to local vaso-motor centers, thence through the splanchnics to the renal ganglia, thence through the renal plexus to the blood-vessels.

The Influence of Variations in the Composition of the Blood.—As it is the function of the kidneys to excrete water, inorganic salts, and various end-products of metabolism from the blood and thus maintain a general average composition, it is highly probable that as soon as they accumulate beyond a certain percentage they themselves act as stimuli to renal activity, either by acting directly on the renal epithelium or by increasing the glomerular pressure. There is evidence at least that urea acts in the former manner and that an excess of water in the blood, from copious drinking or from a sudden checking of the skin from a fall of temperature, acts in the latter manner. The introduction into the blood of inorganic salts, such as potassium nitrate, sodium acetate, etc., will in a short time lead to increased activity of the kidneys, as shown by an increase in the quantity of urine excreted. The manner in which these agents and other members of their class, the so-called saline diuretics, increase renal activity is yet a subject of discussion. On the one hand, it is stated that they promote an absorption of water from the tissues to such an extent that a condition of hydremic plethora is produced, which in itself increases not only the general blood-pressure but the local renal pressure as well, and that it is this factor which is the cause of the increased flow of urine. On the other hand, it is asserted that though the salts increase the local pressure and the volume of the kidney, they nevertheless act specifically on the renal epithelium, and therefore may be regarded as secreto-motor agents. An increase in the percentage of sugar or urea in the blood has a similar influence on the kidney.

The Storage and Discharge of Urine.—Urination.—The urinary constituents, as soon as they are eliminated from the blood, pass into and through the uriniferous tubules and by them are discharged into the pelvis of the kidney. They then enter the ureter by which they are conducted to the bladder. The immediate cause of this movement is undoubtedly a difference of pressure between the terminal portions of the tubules and the terminal portion of the ureter, aided by the peristaltic contraction of the muscle wall of the ureter.

The Bladder.—The *bladder* is a reservoir for the temporary reception of the urine prior to its expulsion from the body. When distended it is ovoid in shape and is capable of holding from 600 to 800 cu. cm. The bladder is composed of four coats: viz., serous, muscle, areolar, and mucous. The muscle coat consists of external longitudinal and internal circular and oblique layers of fibers of the non-striated variety which collectively encircle the entire organ. As these fibers by their contraction expel the urine from the bladder, they are known collectively as the *detrusor urinæ* muscle. At the exit of the bladder the circular fibers are somewhat increased in number, giving rise to the appearance of a distinct muscle band which has been termed the *sphincter vesicæ* muscle. The presence of this muscle has, however, been denied and the retention of the urine has been attributed to mechanic conditions at the neck of the bladder. The urethra just beyond the bladder is provided with a distinct circular muscle composed of striated fibers, the *sphincter urethræ* muscle. At the close of an act of urination or micturition the bladder is small, contracted, and its cavity is almost obliterated, but as urine is continually descending the ureter and entering the bladder at its base, the detrusor muscle gradually relaxes or becomes sufficiently inhibited from moment to moment to receive it. The escape of urine into the urethra is prevented either by mechanic conditions or by the contraction of the sphincter muscle at the vesic orifice. When the accumulating urine reaches a certain volume, it gives rise to an intra-vesic pressure. When this pressure rises to about 80 cm. of water the *detrusor urinæ* acquires a certain degree of tension or tonus. This is followed by rhythmic contractions of the detrusor urinæ which increase in extent and vigor as the urine continues to accumulate until finally a general contraction develops, the force of which overcomes the constricting influences at the bladder orifice and the fluid is discharged. This action of the detrusor muscle is generally reinforced by the contraction of the abdominal muscles. The latter portions of the urine are ejected through the urethra by the rhythmic action of the accelerator urinæ muscles.

The Nerve Mechanism of Urination.—The expulsion of urine is primarily a reflex act though subject to a variable amount of volitional control. The reflex character of the act is especially noticeable in young children in whom, by reason of the imperfect development of the brain, there is a lack of volitional control. During the intervals of urination the orifice of the bladder is closed by the tonic contraction of the sphincter vesicæ and sphincter urethræ muscles, thus preventing the immediate exit of urine after its descent into the bladder. The tonic contraction of both muscles is maintained by the activity of nerve-centers in the lumbar region of the spinal cord. The detrusor muscle is at the same time in a more or less relaxed condition, the result of an inhibition of its governing center in the spinal cord.

When the accumulating urine reaches a certain volume it causes, as previously stated, an intra-vesic pressure, an increased tonus of the detrusor muscle, followed by slight rhythmic contractions of its fibers.

When the desire to urinate is experienced impressions are being made on the afferent nerve endings in the mucous membrane of the bladder. The nerve impulses thus developed are transmitted to the urination center in the spinal cord and to the cerberum and influence in one direction or another their activities. In a young child the arrival of the transmitted impulses in the spinal cord is immediately followed by an inhibition of the sphincter centers and a stimulation of the detrusor center, as a result of which the sphincter muscles relax and the detrusor muscle contracts, thus expelling the urine. In the adult, if the act of urination is to be permitted the same mechanism is brought into action. In its expulsive efforts the detrusor muscle is assisted by the contraction of the abdominal muscles and possibly the diaphragm in response to volitional efforts. After the discharge of urine there is a return to the former condition, namely, a contraction of the sphincter muscles and a gradually inhibition of the detrusor muscle. If the act of urination is to be suppressed volitional impulses descend the cord and cause an increased contraction of the sphincter urethræ muscle, whereby the action of the reflex mechanism is for a while opposed.

The nerve mechanism therefore involves both efferent and afferent nerves as well as nerve-centers in the lumbo-sacral region of the spinal cord.

Efferent Nerves.—The *efferent* nerve-fibers for the sphincter urethræ muscle have their origin in the spinal cord from which they pass by way of the third and fourth sacral nerves, the pelvic nerve and the inferior hemorrhoidal nerve directly to the muscle.

The *efferent* nerve-fibers, for the detrusor muscle, including the specialized portion, the internal sphincter, have their origin in nerve-cells in the lumbo-sacral region of the spinal cord and pass to their destination by two paths. The fibers in the *first* path leave the spinal cord by way of the second to the fifth lumbar nerves, then pass into and through the sympathetic chain, through the *inferior splanchnics* to the inferior mesenteric ganglion around the cells of which their terminal branches arborize; from the cells of this ganglion new fibers emerge which pass through the *hypogastric* nerves to the muscles. The fibers of the *second* path leave the spinal cord by way of the second to the fourth sacral nerves, then pass into the *pelvic* or *erigens* nerve to small ganglia (pelvic ganglia) along the sides of the bladder around the cells of which their terminal branches arborize; from the cells of these ganglia new nerve-fibers emerge which pass directly to the muscles. In both paths the nerves coming from the cord are pre-ganglionic, those coming from the ganglia, post-ganglionic.

The central mechanism that excites and coördinates the activities of the vesical muscles is situated in the lumbo-sacral region of the spinal cord and is designated the vesical or urination center.

Afferent Nerves—The *afferent* nerve-fibers that excite the central mechanism to activity, are contained in both the nerve-paths described in foregoing paragraphs and enter the spinal cord in the dorsal roots of the lumbar and spinal nerves.

Though the origin, course and distribution of the nerves composing this mechanism are fairly well known, their mode of action is somewhat obscure and the results of experimentation not always in accord. According to v. Zeissl stimulation of the peripheral ends of the divided hypogastric nerves causes mainly a contraction of the sphincter muscles and a relaxation of the detrusor muscle, while a stimulation of the peripheral ends of the divided sacral nerves causes a vigorous contraction of the detrusor muscle and a relaxation of the sphincter muscles. The lumbar centers would therefore cause a reception and a retention of the urine, and the sacral centers would cause its expulsion.

PERSPIRATION. SEBUM

The perspiration or sweat, the chief secretion of the skin, is a clear colorless fluid, slightly acid in reaction and saline to the taste. Its specific gravity varies from 1.003 to 1.006. Unless collected from the soles of the feet and the palms of the hand, it is apt to be mixed with epithelial cells and sebum. The total quantity of perspiration secreted daily has been variously estimated at from 700 to 1000 grams; the exact amount, however, is difficult of determination, for the reason that the rate of secretion varies greatly with variations in temperature, food, drink, season of the year, etc.

Chemic analysis of the sweat shows that it contains but from 0.5 to 2.5 per cent. of solid constituents, the variation in the percentage depending on the quantity of water secreted. The solids consist of traces of urea, neutral fats, lactic and sudoric acids in combination with alkaline bases, and inorganic salts (Fovel). Other observers, however, have not been able to detect the presence of either lactic or sudoric acid. Urea is a constant ingredient, though its percentage is extremely small, possibly not more than 0.1 per cent. The amount, however, may be very much increased in uremic conditions, the result of acute or chronic disease of the kidneys. The inorganic constituents consist mainly of sodium chlorid and alkaline and earthy phosphates. Carbonic acid is also present in the free state as well as in combination with alkaline bases.

The very small quantity of the solid constituents in the sweat, taken in connection with the fact that it is excreted most abundantly when the external temperature is high, indicates that it is not so important as an excrementitious fluid as it is as a means for the regulation of the temperature of the body.

The sweat is a product of the secretory activity of specialized glands, the sweat-glands, embedded in the skin, to the histologic structures of which they bear a special relation.

THE SKIN

The skin is a complexly organized structure investing the entire external surface of the body. Its total area varies from 1.17 to 1.35 square meters in man and from 1.1 to 1.17 square meters in woman. It varies in thickness in different localities of the body from $\frac{1}{8}$ to $\frac{1}{100}$ of an inch. The skin consists of two principal layers: viz., a deep layer, the derma or corium, and a superficial layer, the epidermis.

The **derma** or **corium** may be subdivided into a *reticulated* and a *papillary* layer. The reticulated layer consists of white fibrous and yellow elastic tissue, non-striated muscle-fibers, woven together in every direction and forming an areolar network, in the meshes of which are deposited masses of fat and a structureless amorphous matter; the papillary layer consists mainly of club-shaped elevations or projections of the amorphous matter constituting the papillæ. The reticulated layer serves to connect the skin with the underlying structures and to afford support for the blood-vessels, nerves, and lymphatics which are distributed to the papillæ (Fig. 225).

The **epidermis** is an extra-vascular structure consisting entirely of epithelial cells. It may also be subdivided into two layers—the *Malpighian* or *pigmentary* layer, and the *corneous* or *horny* layer. The former is closely applied to the papillary layer of the true skin and is composed of large nucleated cells, the lowest layer of which, the "prickle cells," contains the pigment granules which give to the skin its varying hues in different individuals and in different races of men; the corneous layer is composed of flattened cells which from their exposure to the atmosphere, etc., are hard and horny in texture.

The Sweat-glands.—These glands are tubular in shape, the inner extremity of each being coiled upon itself a number of times, forming a little ball situated in the derma or the subcutaneous connective tissue. From this coil the duct passes up in a straight direction to the epidermis, where it makes a few spiral turns, after which it opens obliquely on the surface. The gland consists of a basement membrane lined with epithelial cells. It is supplied abundantly with blood-vessels and nerves. The sweat-glands are extremely numerous all over the cutaneous surface, though they are more thickly disposed in some situations than others. They probably average 400 to the square centimeter; the total number has been estimated at from 2,000,000 to 2,500,000.

The Influence of the Nerve System on the Production of Sweat.—The secretion of sweat, though a product of the activity of epithelial cells and dependent on a variety of conditions, is regulated to a large extent by the nerve system. Here, as in other secreting glands, the fluid is derived from materials in the lymph-spaces, furnished by the blood. Generally the two conditions, increased blood-flow and increased glandular action, coexist. At times, however, a profuse clammy perspiration is secreted with diminished blood-flow. Two sets of nerves are evidently concerned in this process: viz., *vaso-motor nerves*, which regulate the blood-supply, and *secretor* nerves, which stimulate the gland-cells to activity.

The Sweat Nerves.—The sweat nerves which excite the activities of the epithelium of the sweat-glands have their origin in nerve-cells located in the anterior and lateral gray matter of the spinal cord. The sweat nerves, like the vaso-motor nerves, do not pass directly to the gland-cells, but indirectly by way of the ganglia of the sympathetic chain. In these ganglia the sweat nerves terminate, their end-branches aborizing around the nerve-cells. From the cells of these ganglia new nerve-fibers arise which then pass without interruption to their final destination. The former are termed pre-ganglionic, the latter post-ganglionic. From their origin and distribution it is apparent that the sweat nerves are constituent portions of the autonomic nerve system.

From experiments made on animals and from observation of clinic conditions in human beings, it may be stated in a general way, that the pre-ganglionic fibers which emerge from the spinal cord in the ventral roots of spinal nerves between the second thoracic and third lumbar nerves may be divided into four groups, viz.: (1) Those distributed to the sweat-glands of the skin of the trunk of the body; (2) those for the sweat-glands of the fore limbs; (3) those for the sweat-glands of the head, neck and face; (4) those for the sweat-glands of the hind limbs. These nerves pursue the same route as the vaso-motor nerves with which they are associated in function (see page 377).

The exact course for the sweat nerves has been experimentally determined only for the cat and dog. In these animals, however, sweat-glands are found only in the balls of the feet. According to Langley's observations the sweat nerves for the forefeet leave the spinal cord in the thoracic nerves from the fourth to the tenth inclusive. After passing into the sympathetic chain they ascend to the stellate ganglion, around the cells of which their end-branches arborize. From this ganglion non-medullated fibers pass in the gray rami communicantes to the nerves composing the brachial plexus and then to the feet. The sweat nerves for the hind feet leave the cord mainly in the first and second lumbar and terminate in sympathetic ganglia, from which the post-ganglionic nerves pass into the nerve-trunks included between the sixth lumbar and the second sacral nerves, which enter into the formation of the sacral plexus and through which they pass to the feet.

The existence of a dominating sweat center in the medulla oblongata is probable, though its location has never been definitely determined.

That the sweat-glands are stimulated to activity by nerve impulses is shown by the fact that stimulation of the peripheral ends of the divided cervical sympathetic, of the brachial plexus, or of the sciatic nerve is followed in a few seconds by a profuse secretion. Though under physiologic conditions there is a simultaneous dilatation of the blood-vessels and an increased supply of blood, this is merely a condition and not a cause of the secretion; for the secretion can be excited and the flow maintained for a period of from ten to fifteen minutes after ligation of the blood-vessels of the limb or even after its amputation, when the corresponding nerve is stimulated.

As the sweat-glands are always in a state of more or less activity it is assumed that the sweat centers possess a certain degree of tonicity, though the cause for such tonicity has not been made apparent. It is quite possible that the presence of carbon dioxid in the blood, as well as the temperature, may be important factors, since an increase in the venosity of the blood or a rise in temperature is usually followed by an increase in the amount of sweat excreted. The centers may also be excited to increased activity by both central and peripheral causes, *e.g.*, psychic states of an emotional character and a rise in the external temperature. Pilocarpin injected into the blood causes a profuse secretion even when the nerves have been divided. Its action is supposed to be exerted on the terminal branches of the nerves and possibly on the cells themselves. As in the case of the salivary glands atropin suspends the activity of the terminal branches of secretor nerves.

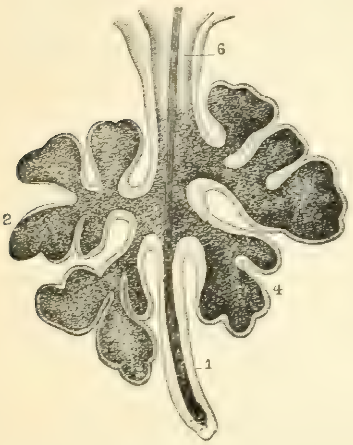

Fig. 214.—Large Sebaceous Gland. 1. Hair in its follicle. 2, 3, 4, 5. Lobules of the gland. 6. Excretory duct traversed by the hair. —(*Sappey.*)

Hairs.—Hairs are found in almost all portions of the body, and can be divided into—

1. Long, soft hairs, on the head.
2. Short, stiff hairs, along the edges of the eyelids and nostrils.
3. Soft, downy hairs on the general cutaneous surface.

They consist of a *root* and a *shaft.* The shaft is oval in shape and about 60 micromillimeters in diameter; it consists of fibrous tissue, covered externally by a layer of imbricated cells, and internally by cells containing granular and pigment material.

The *root* of the hair is embedded in the hair-follicle, formed by a tubular depression of the skin, extending nearly through to the subcutaneous tissue; its walls are formed by the layers of the corium, covered by epidermic cells. At the bottom of the follicle there is a papillary projection of amorphous matter, corresponding to a papilla of the true skin, containing blood-vessels and nerves, upon which the hair-root rests. The investments of the hair-roots are formed of epithelial cells, constituting the *internal* and *external* root-sheaths.

The lower portion of the hair-follicle is connected with the upper surface of the derma by bundles of non-striated muscle-fibers which are termed *arrectores pilorum* muscles. Their inclination and insertion are such that their contraction is followed by erection of the hair-follicle and hair-shaft. These muscles are excited to action by nerves termed *pilo-motor* nerves.

THE SEBUM

The **sebum** or **sebaceous matter** is a peculiar oily material produced by specialized glands in the skin. It consists of water, epithelium, proteids, fat, cholesterin, and inorganic salts.

The **sebaceous glands** are simple and compound racemose glands opening by a common excretory duct on the surface of the epidermis or into the shaft of a hair-follicle (Fig. 214). These glands are extremely numerous and found in all portions of the body, with the exception of the palms of the hands and soles of the feet, and most abundantly in the face. They are formed by a delicate structureless membrane lined by polyhedral epithelium.

The sebum is not produced by an act of true secretion, but is formed by a proliferation and degeneration of the gland epithelium. When first poured on the surface, the sebum is oily and semiliquid in character, but soon hardens and acquires a cheese-like consistence. It serves to lubricate the hair and skin and prevent them from becoming dry and harsh.

The surface of the fetus is generally covered with a thick layer of sebaceous matter, the *vernix caseosa*, which possibly keeps the skin in a normal condition by protecting it from the effects of the long-continued action of the amniotic fluid in which the fetus is suspended.

CHAPTER XVIII

EXTERNAL SECRETIONS

Secretion is a term applied to a process by which complex fluids are formed from the constituents of the lymph which are separated from the blood-stream by the activities of the endothelial cells of the capillary wall, as the blood flows through the capillary blood-vessels. In this process the endothelial cell is aided by the physical forces, diffusion, osmosis, and filtration. These separated materials may be utilized in several ways:

1. For the repair of the tissues, for growth, for the liberation of energy.
2. For the elaboration or production by specialized organs of a variety of complex fluids and specific materials of widely different application. The fluids and specific materials thus formed are utilized for the most part to meet some special need of the body. All such fluids and materials are termed *secretions*, and the organs by which they are formed are termed secretor organs. Secretions whether simple or complex may in a general way be divided into two groups, viz.: external and internal.

External Secretions.—An external secretion may be defined as a more or less complex fluid formed by the secretor activities of epithelial cells of glands, which is discharged through well-defined ducts on the surfaces of the body, the skin or mucous membrane. The glands by which they are formed or secreted are known as glands of *external* secretion.

Internal Secretions.—Internal secretions may be defined as more or less complex materials or agents formed by the activities of epithelial cells of organs, and which are discharged into, and distributed by the blood to organs and tissues near and remote, the activities of which they influence in varying ways and degrees. The glands by which they are formed or secreted are known as glands of *internal* secretion.

Organs of External Secretions.—All organs belonging to this group consist primarily of a thin delicate homogeneous membrane, one side of which is covered with a layer of epithelial cells and the other side of which is closely invested by a network of capillary blood-vessels, lymph-vessels, and nerves. Though the epithelial cells have a general histologic resemblance one to another, their physiologic function varies in different situations, in accordance probably with their ultimate chemic structure, a fact which determines the difference in the character of the secretions.

These organs may consist of a single layer of cells or a group of cells, and may be subdivided into—

1. Secreting membranes.
2. Secreting glands.

The **secreting membranes** are the mucous membranes lining the gastro-intestinal, the pulmonary, and the genito-urinary tracts, and the serous membranes lining closed cavities, such as the pleural, pericardial, peritoneal, and synovial membranes.

The *mucous membranes* are soft and velvety in character and are composed of a condensed connective tissue forming a basement membrane beneath which is a layer of blood-vessels and muscle-fibers, and on which is a layer of epithelium, the histologic as well as physiologic characters of which vary in different situations. The mucus secreted by the various epithelial forms will very naturally possess a somewhat different composition, according to the locality in which it is formed. In a general way it may be said that mucus is a pale, semi-transparent, alkaline fluid, containing leukocytes and epithelial cells. It is composed chemically of water, mineral salts and an albuminoid body, *mucin*, to the presence of which it owes its viscidity. Much of the mucus is secreted by the goblet cells on the surface of the mucous membranes. The principal varieties of mucus are the nasal, bronchial, vaginal, urinary, and gastro-intestinal.

The *serous membranes* are composed of thin membrane formed by a condensation of connective tissue and covered by a single layer of large, flat, nucleated cells with irregular margins. These membranes enclose what are practically large lymph-sacs or spaces, and the fluid they contain resembles lymph in all respects and is practically identical with it. It serves to diminish friction when the viscera they enclose move over one another. The most important of the serous membranes are the pleural, pericardial, and peritoneal.

The *synovial membranes* in and around joints resemble serous membranes. The cells covering them, however, secrete a clear, colorless fluid resembling lymph, but differing from it in containing a mucin-like substance, a nucleo-albumin, which imparts to it considerable viscidity. This synovial fluid serves to diminish friction between the opposing surfaces of the bones as they glide over one another during movement.

Other secretions, such as the aqueous and vitreous humors of the eye, the fluid of the internal ear, the cerebrospinal fluid, etc., will be considered in connection with the organs with which they are associated.

The **secreting glands** are formed of the same histologic elements as the secreting membranes. They are formed by an involution of the mucous membrane or skin, the epithelium of which is variously modified structurally and functionally in the various situations in which they are formed. Like the membranes themselves, the glands are invested by capillary blood-vessels and supplied with lymph-vessels and nerves, of which the latter are in direct connection with the blood-vessels and epithelial cells. The interior of each gland is in communication with the free surface by one or more passageways known as ducts.

These glands may be classified according as the involution is cylindrical or dilated as—

1. Tubular. The *tubular* glands may be simple—*e.g.*, sweat-glands, intestinal glands, fundus glands of the stomach; or compound—*e.g.*, kidney, testicle, salivary, and lachrymal glands.

2. Alveolar. The *alveolar* glands may also be simple—*e.g.*, the sebaceous glands, the ovarian follicles, meibomian glands; or compound, as the mammary glands and salivary glands.

For the production of a secretion it is necessary that the plasma of the blood, the common material, be delivered to the lymph-spaces with which the epithelial cells are in close relation. The processes involved in the passage of the plasma across the capillary wall have already been considered in connection with the production of lymph. They include the physical processes, diffusion, osmosis, and filtration combined with a secretor activity of the cells of the capillary wall. The question as to which of these processes is the more active is yet a subject of investigation.

As the chemic composition and the chemic features of the organic constituents of all secretions have been demonstrated to be the outcome of metabolic processes going on within the epithelial cells, it must be assumed at least that these differences are correlated with differences in the histologic features and chemic composition of the epithelium. The discharge of the secretion is, as a rule, intermittent; that is, there are periods of inactivity or rest. In rest more especially the epithelial cells, after the assimilation of lymph, accumulate within themselves such characteristic products as globules of mucin, granules which apparently are the antecedents of the digestive enzymes, granules of glycogen, globules of fat, sugar, and proteins, as in the case of the mammary gland. In how far all these compounds are the result of secretor activity or of a cell degeneration and disintegration it is impossible to state in the light of present knowledge. During the period of gland rest the blood-supply to the gland is merely sufficient for nutritive purposes. When the occasion arises for gland activity, the blood-vessels, under the influence of the vaso-motor nerves, dilate and deliver to the gland an amount of blood far beyond that required for nutritive purposes. As a result the gland becomes red and vascular and the blood emerging by the veins frequently retains its customary arterial color. The increased blood-supply favors a rapid transudation of water and salts into the lymph-spaces from which they are speedily absorbed and transmitted by the epithelial cells into the interior of the gland lumen. Coincident with the passage of water through the cell, the organic constituents are extruded from the end of the cell bordering the lumen to become dissolved, or in the case of fat to be suspended, in the water. The secretion thus formed accumulates and with the rise of pressure which inevitably follows it at once passes into the ducts to be discharged on the surface of the mucous membrane or skin, as the case may be.

The Influence of the Nerve System.—The activity of every gland is controlled by nerve-centers situated in the central nerve system. These centers may be excited to activity either by impressions made on the peripheral terminations of afferent nerves or by emotional states, or, possibly, by changes in the composition of the blood itself. As a rule, all normal secretion is a reflex act involving the usual mechanism: viz., a receptive surface (skin, mucous membrane, or sense-organ), an afferent nerve, an emissive cell from which emerges an efferent nerve to be distributed to a responsive organ, the gland epithelium, though the secretion may in some instances be initiated by a psychic state.

For the production of the secretion by the epithelial cell it is believed by some experimenters that two physiologically distinct, efferent nerve-fibers are involved—one stimulating the production of the organic constituents (*trophic* nerves), the other stimulating the secretion of water and inorganic salts (*secretor* nerves). The evidence for the influence of the nerve system on secretion and the mode of connection of the nerve-fibers with the gland-cells have been alluded to (page 156) and will again be in subsequent chapters.

The structure of the glands of external secretion, the composition and physiologic actions of their secretions have in large part been considered in the foregoing chapter on Digestion. There remains, however, to be considered the mammary glands, the liver and the sebaceous glands.

MAMMARY GLANDS

The **mammary glands,** which secrete the milk, are two more or less hemispheric organs situated in the human female on the anterior surface of the thorax. Though rudimentary in childhood, they gradually increase in size as puberty approaches. The gland presents at its convexity a small conical eminence termed the mammilla or nipple, surrounded by a circular area of pigmented skin, the areola. The gland proper is covered by a layer of adipose tissue anteriorly and is attached posteriorly to the pectoral muscles by a network of fibrous tissue.

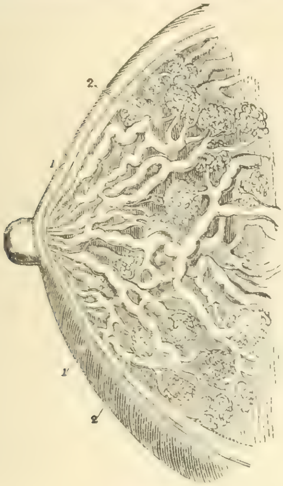

FIG. 215.—MAMMARY GLAND. 1. Lactiferous ducts. 2. Lobuli of the mammary gland.

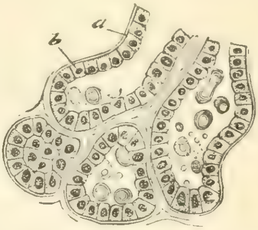

FIG. 216 —ACINI OF THE MAMMARY GLAND OF A SHEEP DURING LACTATION. *a*. Membrana propria. *b*. Secretory epithelium.

During utero-gestation the mammary glands become larger, firmer, and more lobulated; the areola darkens and the blood-vessels, especially the veins, become more prominent. At the period of lactation the gland is the seat of active histologic and physiologic changes correlated with the production of milk. At the close of lactation these activities cease, the glands diminish in size, undergo involution, and gradually return to their former non-secreting condition.

Structure of the Mammary Gland.—Each mammary gland consists of an aggregation of some 15 or 20 irregular pyramidal lobes, each of which is surrounded by a framework of fibrous tissue. This tissue affords support for blood-vessels, lymph-vessels, and nerves. Each lobe is provided with a single excretory duct, the lactiferous duct, which as it approaches the areola expands into a fusiform ampulla or reservoir. At the base of the nipple the ampullæ contract to form some 15 or 20 narrow ducts, which, ascending the nipple, open by constricted orifices 0.5 mm. in diameter on its apex (Fig. 215).

On tracing the lactiferous duct into a lobe, it is found to divide and subdivide into a number of branches, which pass into smaller masses—the lobules. The lobule in turn is composed of a large number of tubular acini or alveoli, the final terminations of the lobular ducts. Each acinus consists of a basement membrane lined by a single layer of low cuboidal epithelial cells (Fig. 216). Externally the acinus is surrounded by blood-vessels, nerves, and lymphatics.

MILK

Physical Properties.—Milk as obtained during active lactation is an opaque bluish-white fluid, almost inodorous, with a sweet taste, an alkaline reaction, and a specific gravity of from 1.025 to 1.040. Examined microscopically, it is seen to consist of a clear fluid, the milk *plasma*, holding in suspension an enormous number of small, highly refractive oil-globules, which measure on the average about $\frac{1}{1000}$ of an inch in diameter. It has been asserted by some observers that each globule is surrounded by a thin protein envelope which enables it to maintain the discrete form. This, however, is at present disbelieved.

The quantity of milk secreted daily by the human female averages about 1200 c.c.

Chemic Composition.—The chemic analysis of milk shows that it consists of all the different classes of nutritive principles, which are necessary to the growth and development of the body. The only exception appears to be an insufficient amount of iron (3 or 4 milligrams per 1000 grams of milk) for the formation of the coloring matter of the blood, the hemoglobin. This is provided, however, by the liver in which the iron accumulates during intra-uterine life. According to Bunge the liver of a rabbit newly born contains as much as 18.2 milligrams per 100 grams of body-weight, while at the end of twenty-four days it contains only 3.2 milligrams per 100 grams of body-weight. The composition, however, varies not only in different classes of mammals but in the same animal at different times and under different physiologic conditions. Average compositions of milk of certain animals are shown in the following table:

THE COMPOSITION OF MILK

Constituents	Human	Cow	Goat	Mare	Ass
Water	87.80	87.00	86.91	90.00	90.00
Caseinogen	1.50	3.20	3.69	1.80	2.10
Lactalbumin				0.30	
Fat	3.50	3.80	4.09	1.30	1.30
Lactose	7.00	5.00	4.45	5.50	6.30
Inorganic Salts	0.20	0.50	0.86	0.30	0.30

Caseinogen is the chief protein constituent of milk. Associated with it, however, are two other proteins, lactalbumin and lactoglobulin, both of which are present in but small quantity. When milk is treated with acetic acid, sodium chlorid, or magnesium sulphate to saturation, the caseinogen is *precipitated* as such, and after the removal of the fat with which it is entangled may be collected by appropriate chemic methods. On the addition of rennet, an alcoholic extract of the mucous membrane of the calf's stomach, which contains the enzyme *rennin* or *pexin*, the caseinogen undergoes a conversion into an insoluble protein, casein or tyrein. To this process the term *coagulation* has been given. The presence of calcium phosphate appears to be essential to this process, inasmuch as it does not take place if the milk be completely decalcified by the addition of potassium oxalate. After coagulation, the more or less solid mass of milk separates into a liquid portion, the serum, and a solid portion, the coagulum. The former, generally termed whey, consists of water, salts, lactalbumin, sugar; the latter, the curd, consists of the casein and entangled fat. Boiling the milk retards and even prevents the coagulation by rennet, owing to the precipitation of the calcium phosphate. When milk is taken into the stomach, it is probable that the rennin coagulates the caseinogen in a manner similar to, if not identical with, this process, which appears to be essential to the normal digestion of the milk.

Fat is present in the condition of a very fine emulsion and is more or less solid at ordinary temperatures. It is a compound of olein, palmitin, and stearin with small quantities of butyrin and caproin. The melting-point of butter varies between 31° and 34°C. When milk is allowed to stand for some time, the fat-globules rise to the surface and form a thick layer known as cream. Churning the milk or cream causes the fat-globules to run together and form a coherent mass termed butter.

Lactose is the particular form of sugar characteristic of milk. It belongs to the saccharose group and has the following composition: $C_{12}H_{22}O_{11}$. Though incapable of undergoing fermentation by the action of the yeast plant it is readily reduced by the *Bacillus acidi lactici* to lactic acid and carbon dioxid, the former of which imparts to milk an acid reaction and a sour taste. With the accumulation of the lactic acid the caseinogen is precipitated as a more or less consistent mass.

Inorganic salts are always present and are chiefly those of potassium, sodium, calcium, and magnesium phosphates and chlorids. The following table of Bunge gives the quantitative amounts of these constituents in both human and cow's milk:

In 1000 Parts	Potassium	Sodium	Calcium	Magnesium	Iron Oxid	Phosphoric Acid	Chlorin
Human milk	0.78	0.25	0.33	0.06	0.0036	0.47	0.43
Cow's milk	1.76	1.11	1.59	0.21	0.0030	1.97	1.69

Iron is also present in small amounts possibly from 3 to 5 milligrams per 1000 c.c. Citric acid to the extent of 0.05 per cent. is also present.

Mechanism of Milk Secretion.—During the time of lactation the mammary gland exhibits periods of secretory activity which alternate with periods of repose. Coincidently with these periods certain histologic changes take place in the secreting epithelium. At the close of a period of active secretion and after the discharge of the milk each acinus presents the following features: The epithelial cells are short, cubical, nucleated, and border a relatively wide lumen, in which is found a variable quantity of milk. After the gland has rested for some time active metabolism again begins. The cells grow and elongate; the nucleus divides into two or three new nuclei; constriction takes place and the inner portion is detached and discharged into the lumen of the acinus. During the time these changes are taking place oil-globules make their appearance in the cell protoplasm, some of which are discharged separately into the lumen, while others remain for a time associated with the detached portion of the cell (Fig. 217). From these histologic changes it is inferred that the caseinogen and fat are products of the metabolism of the cell protoplasm and not derived directly from the lymph from the blood. The lactose apparently has a similar origin, as appears from the fact that it is not found either in the blood or any other tissue, and that it is formed independently of carbohydrate food. The water, and especially the inorganic salts, are the result of secretor activity rather than of diffusion and filtration. This is rendered probable from the fact that the proportions of the inorganic salts of milk are more closely allied to those of the tissues of the new-born child than to blood. With the passage of the water and salts into the lumen of the acinus the proteids undergo disintegration and solution and the liquid assumes the characteristics of milk.

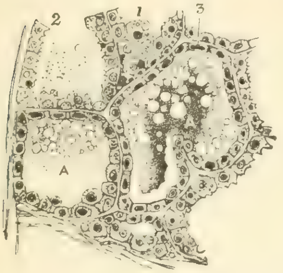

Fig. 217.—Section of the Mammary Gland of a Cat in the Early Stages of Lactation. A. Cavity of alveoli filled with granules and globules of fat. 1, 2, 3. Epithelium in various stages of milk-formation.—(*Yeo.*)

The discharge of milk is occasioned by the suction efforts on the part of the child, aided by atmospheric pressure and the contractions of the non-striated muscle-fibers of the lactiferous ducts.

The Developmental Changes and the Secretion of Milk.—Previous to menstruation the glands are quite rudimentary, but with the establishing of this function they increase in size as a result of the growth of connective tissue and the deposition of fat. The glandular tissue is, however, more or less inactive, but with impregnation it too undergoes a rapid development. The alveoli increase in number and size and toward the end of the period of pregnancy begin to secrete the forerunner of milk, the fluid colostrum. From the foregoing it is apparent that there is a close relationship between the activities of the ovaries and the uterus and the activities of the mammary glands though the mechanism by which the two groups of activities are mediated is not very clear. Starling and Lane-Claypon have thrown some light on the mechanism by the demonstration that the injection of water extracts of developing feti into the body of a non-pregnant mammal—a rabbit—for a period of from 15 to 17 days was followed by the development of the mammary glands, similar if not identical with the development that occurs during an actual pregnancy. From this fact the inference is drawn that during intra-uterine life, the fetus as it develops secretes an agent which, entering the maternal blood, is carried to the mammary glands and by it stimulated to growth. The agent thus produced by the fetus would belong to the class of agents known as hormones. Since those katabolic changes in the cells of the glands which eventuate in the formation of milk do not arise during the intra-uterine life of the fetus, but which soon arise after birth, the further assumption is made that this hormone has an inhibitor influence on the gland-cells which prevents the formation of milk; but with its withdrawal after birth secretion at once begins.

Influence of the Nerve System.—Judging from analogy, it is probable that the secretion of milk is regulated by impulses emanating from the nerve system, though the exact nerve-channels for the transmission of such impulses have not been determined experimentally. The results of experiments made on the nerve distribution to the mammary gland of the goat are unsatisfactory and contradictory and do not shed much light on the subject. Even after division of all nerves to this gland in this animal, secretion continues in an apparently normal manner. Nevertheless, it is well known that emotional states on the part of the mother modify the quantity as well as quality of milk, indicating a connection between the gland-cells and the central organs of the nerve system. Nerve terminals have been discovered in and around the epithelial cells—a fact which supports this view.

Colostrum.—Within a day or two after parturition the alveoli become filled with a fluid which in some respects resembles milk and which has been termed colostrum. This is a watery fluid containing disintegrated epithelial cells and fat-globules, as well as a colostrum corpuscles, which are probably leukocytes containing fine fat-globules. Colostrum is distinguished from milk in being richer in sugar and inorganic salts. It also differs from milk in undergoing coagulation by heat which is supposed to be due to the presence of a globulin. Its coagulation point is about 72°C. It is said to possess constituents which act as a laxative to the young child.

THE LIVER

The **liver** is a large gland situated in the upper and right side of the abdominal cavity, where it is held in position largely by ligaments formed by reduplications of the peritoneal investment. In the adult it weighs, freed of blood, from 1300 to 1700 grams. The liver is connected with the duodenal portion of the intestine by the hepatic duct. It receives blood both from the hepatic artery and from the portal vein, and in this respect differs from all other glands in the body. The epithelial structures of the liver are inclosed by a firm fibrous membrane, known as Glisson's capsule. At the transverse fissure it invests and follows the blood-vessels, which there enter, in all their ramifications through the gland.

Structure of the Liver.—The liver is composed of an enormous number of small masses, rounded, ovoid, or polygonal in shape, called lobules, measuring about one millimeter in diameter and separated from one another by a narrow space in which are to be found blood-vessels, lymphatics, and hepatic ducts, supported by connective tissue. In the pig this space and its contained elements is quite distinct, sharply marking out the border of the lobule (Fig. 218). This is not so apparent in man. Each lobule is made up of irregular or polygonal-shaped cells measuring about 30 to 40 micromillimeters in diameter. These cells are arranged in a radial manner from the center to the circumference of the lobule (Fig. 219). Each cell possesses one and at times two nuclei. There is no evidence for the existence of a distinct cell-wall. The cell protoplasm frequently contains globules of fat, granules of a protein nature, granules of glycogen, pigment material, etc. The appearance presented by the cell will vary considerably, according to the time it is observed. Thus there may be a complete absence of these constituents, when the cell may present a series of vacuoles separated by bands of protoplasm. The cells are the secreting structures of the liver, and hence are in close relation to capillary blood-vessels, lymph spaces, nerves, and irregular channels or passageways. The latter running between the epithelial cells may be compared to the lumen of other secreting glands.

Blood-vessels and Their Distribution.—The blood-vessels which are in relation with the liver are:

1. The portal vein.
2. The hepatic artery.
3. The hepatic vein.

The portal vein and the hepatic artery enter the liver at the transverse fissure. After penetrating its substance they divide and subdivide into smaller and smaller branches, which ulimately occupy the space between the lobules, completely surrounding and limiting them. From their situation they are termed *interlobular* veins and arteries.

The interlobular veins give off small capillary vessels which penetrate the lobule at all points of its surface. These capillaries, though frequently anastomosing, form a radial meshwork which converges toward the center of the lobule. In the meshes of this plexus are found, arranged in a corresponding radial manner, the liver cells. The interlobular arteries are distributed to the walls of the portal vein, to the connective tissue, and finally terminate in the portal vein capillaries. The intralobular capillaries thus receive and transmit blood which is an admixture of both arterial and venous blood. In the center of each lobule there is a large vein, formed by the union of the intralobular capillaries, known as the *intralobular* vein, which collects all the blood of the lobule and transmits it through the lobule to an underlying or sublobular vein (Fig. 220). These latter vessels, uniting and reuniting, ultimately form the hepatic vein, which empties the blood into the inferior vena cava.

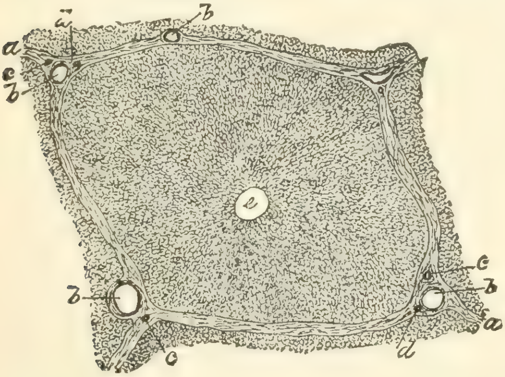

FIG. 218.—SECTION OF LIVER OF PIG, SHOWING VERY DIAGRAMMATICALLY THE LOBULES. *a*. Interlobular connective tissue. *b, c*. Branches of portal vein and of hepatic artery. *d*. Bile-ducts. *e*. Intralobular vein.—(*Piersol.*)

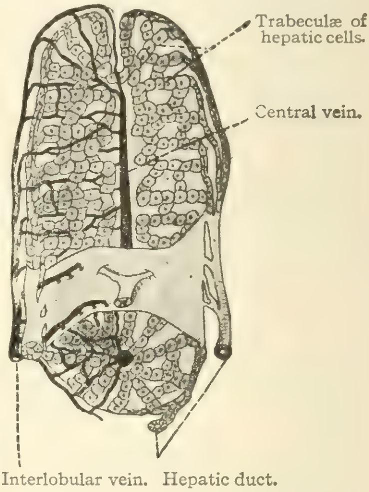

FIG. 219.—SCHEME OF A HEPATIC LOBULE, REPRESENTED IN TRANSVERSE SECTION BELOW AND, BY PARTIAL LEVELING, IN LONGITUDINAL SECTION ABOVE. In the left half the blood-vessels are drawn; in the right half only the cords of hepatic cells. × 20. —(*Stöhr.*)

Bile Capillaries and Hepatic Ducts.—The bile capillaries are narrow channels which penetrate the lobule in all directions and are generally found running along the sides of the cells. These channels, which are devoid of walls, receive from the cells some of the products of their secretor activity, and hence are comparable to the lumen of the alveoli of other secreting glands. At the periphery of the lobules the bile capillaries communicate with larger channels which are the beginnings of the hepatic or bile-ducts lying in the interlobular spaces. The interlobular bile-ducts possess a distinct wall lined by flattened epithelium. There is, however, no distinct line of demarcation between the cells of the interlobular ducts and the secreting cells of the liver proper, as the two blend insensibly, the one into the other. As the hepatic ducts increase in size they gradually acquire the structure characteristic of the main hepatic duct: viz., a mucous, a muscle, and a fibrous coat.

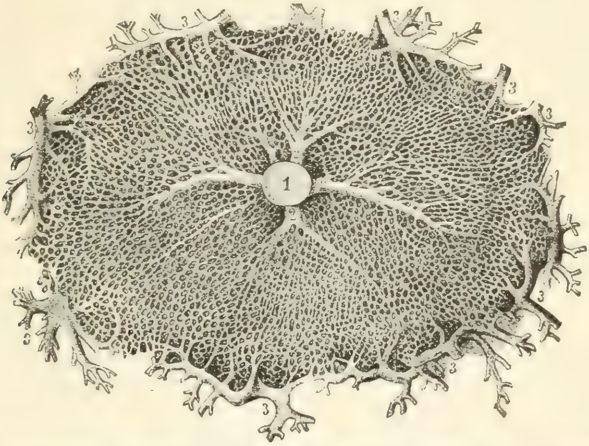

FIG. 220.—TRANSVERSE SECTION OF A SINGLE HEPATIC LOBULE. 1. Intralobular vein, cut across. 2, 2, 2, 2. Afferent branches of the intralobular vein. 3, 3, 3, 3, 3, 3, 3, 3, 3. Interlobular branches of the portal vein, with its capillary branches, forming the lobular plexus, extending to the radicles of the intralobular vein.—(*Sappey.*)

The Nerve Supply.—Experimental investigations have demonstrated that the liver is supplied with nerves derived from the central nerve system. The route of these nerves is probably by way of the vagi and of the splanchnics as far as the semilunar ganglion, around the cells of which the terminal fibers arborize. From the cells of this ganglion post-ganglionic fibers arise which pass by way of the hepatic plexus along the course of the hepatic artery and portal vein. Many of the nerves which enter the liver are vasomotor in function; as to whether others are secretor in character is yet a subject of investigation. It has been asserted that nerve filaments have been demonstrated running between the cells and even penetrating their substance. This fact would indicate that the metabolic processes of the liver are under the control of the central nerve system.

Functions of the Liver.—The anatomic and histologic peculiarities of the liver would indicate that it has a variety of relations to the general processes of the body. Experimental investigation has brought some of these relations to light. Though its physiologic actions are not yet wholly understood, it may be said that it is engaged in:

1. The elaboration and excretion of bile.
2. The production of starch (glycogen) and sugar (glucose).

3. The formation of urea.
4. The conjugation of products of protein putrefaction.

The Elaboration of Bile.—The physical properties and chemical composition of the bile have already been considered (page 195). The characteristic salts of the bile, sodium glycocholate and taurocholate, do not pre-exist in the blood, and therefore must be formed by the liver cells out of materials derived from the blood of the intralobular capillaries. The antecedents of the bile salts, glycocoll and taurin, are crystallizable nitrogenized compounds, and known chemically as amido-acetic and amido-ethylsulphonic acids. Their chemic composition indicates that they are derivatives of the proteins, though the intermediate stages in their production are unknown. The origin of the cholalic acid with which they are combined is equally obscure. The bile salts as they are found in the bile are produced however in the liver cells by metabolic activity.

The primary coloring-matter of the bile, bilirubin, has been shown to be a derivative of hematin, a product of the disintegration of hemoglobin. It is supposed that the liver cells bring about this change by combining water with hematin, with the abstraction of iron. The product thus formed is bilirubin, which is excreted, while the iron is for the most part retained in the liver cells.

Cholesterin is a waste product derived largely from the nerve-tissue. It is brought to the liver and simply excreted by the cells. The remaining constituents of the bile, water and inorganic salts, are secreted here in the same way as in all other glands.

When once formed, the liver cells discharge these various compounds into the channels by which they are surrounded; they then pass into the open mouths of the bile-ducts at the periphery of the lobules. Under the increasing pressure which arises from the secretion and accumulation of bile, this fluid flows from the smaller into the larger bile-ducts, and finally is emptied either directly into the intestine or into the gall-bladder, where it is stored until required for digestive purposes. The secretion of bile, as observed by means of a biliary fistula, is continuous and not intermittent, though the rate of flow is subject to considerable variation.

The liver cells, as far as the secretion of bile is concerned, appear to be independent of the nerve system. Their activity, however, is stimulated by the increased blood-supply which arises during digestion in consequence of the dilatation of the intestinal vessels, since it is at this period that the rate of discharge is the greatest. The same results have been shown by experiment. Thus, division of the splanchnic nerves is followed by an increased discharge of bile, apparently due to the dilatation of the portal vessels; stimulation of their peripheral ends is followed by a decreased discharge of bile in consequence of the contraction of the portal vessels. The bile salts appear to be the most efficient stimulants to the activity of the liver cells, for their administration and absorption is followed by an increase not only in the amount of water, but of the inorganic salts and other solid constituents as well.

The flow of bile from the bile capillaries to the main hepatic duct, though primarily dependent on differences of pressure, is aided by the contraction of the muscular walls of the bile-ducts and the inspiratory movements of the diaphragm. Any obstacle to the discharge of bile leads to its accumulation, a rise of pressure beyond that of the capillary blood-vessels, and a reabsorption by the lymph-vessels of the bile constituents. After their discharge into the blood from the thoracic duct these constituents are deposited in part in various tissues, giving rise to the phenomena of jaundice, and in part are eliminated in the urine.

The Production of Starch (Glycogen) and Sugar (Glycose or Glucose).—In 1857 Bernard discovered the fact that the liver normally during life produces a substance, analogous in its chemic composition to starch and known as liver starch or animal starch. This substance can be obtained by the following method: Small pieces of the liver of an animal recently killed, preferably after a meal rich in carbohydrates, are placed in acidulated boiling water for a few minutes; then rubbed up in a mortar with sand, again boiled, after which the proteins are removed by filtration. The filtrate thus obtained is opalescent and resembles a solution of starch. The starch may be precipitated from this solution with alcohol. It may subsequently be obtained free by drying, when it presents itself as a white amorphous powder, soluble in hot or cold water. Chemic analysis shows that it consists of $C_6H_{10}O_5$, or a multiple of it.

When either the original solution obtained by boiling or a solution of this amorphous powder is treated with iodin, it strikes a port-wine color. When digested with saliva, pancreatic juice, or boiled with dilute acids, the solution becomes clear, and testing with Fehling's solution reveals the presence of sugar.

For the reason that this starch is capable of being transformed into or of generating glycose or glucose it received the name of glycogen; and inasmuch as the liver continually produces glycogen it may be said to have a starch-forming or an *amylogenetic* or a *glycogenic* function.

If the liver be allowed to remain in the body of an animal for a period of twenty-four hours before the decoction is made as above described, it will be found that the solution contains only a small amount of starch but a relatively large amount of sugar. The inference drawn is that after death the starch is transformed by some agent, possibly a ferment, into sugar (glucose). From this fact as well as from the results of different lines of investigation, it is the generally received opinion that the same change is constantly taking place in the living condition and therefore the liver is said to have a sugar-forming or a *glycogenetic* function. The liver cells are thus characterized by two processes *amylogenesis* and *glycogenesis*. To the transformation of glycogen into sugar the term *glycogenolysis* has recently been applied.

The presence of glycogen in the liver cells can be shown microscopically in the form of discrete hyaline and refractive masses, which show a blue or violet color with iodin. As they are soluble in water they can be readily dissolved out from the cells, leaving small vacuoles separated from one another by strands of cell substance. The amount of glycogen in a well-fed animal varies from 1.5 to 4 per cent. of the total weight of the liver. By experimental methods it has been shown that the production of glycogen is dependent very largely on the consumption of carbohydrates, the greater the amount of sugar and starch in the food, the greater being the production of glycogen. Nevertheless it is also certain that glycogen can be derived from proteins; for if the carbohydrates are excluded from the food and the animal fed on a pure protein diet plus fat, glycogen will continue to be formed in the liver though in far less amounts.

The facts connected with the formation of glycogen, as well as with its transformation as at present generally accepted, may be stated as follows: The dextrose or glucose into which the carbohydrates are mainly converted by the action of the digestive fluids is absorbed into the blood of the portal vein and carried direct to the liver, where a certain portion of it diffuses across the capillary walls into the surrounding lymph-spaces; by the action of the cells or by a special enzyme it is then dehydrated, and temporarily deposited under the form of the non-diffusible body glycogen. At a subsequent period and in proportion to the needs of the system the liver cells, through the agency of a ferment, transform the glycogen into glucose or dextrose by the addition of a molecule of water, after which it is returned to the blood, by which it is transported to the systemic capillaries, where it disappears again, diffusing across the walls of the capillaries into the surrounding lymph-spaces to play a part in the general nutritive process. Though the final disposition of the sugar is uncertain it is highly probable that after its delivery to the muscles, for example, it may be directly oxidized or temporarily stored as glycogen or possibly be used in the formation of living material. Ultimately, however, through oxidation *(glycolysis)* it yields heat and contributes to the production of muscle energy. Should there be a failure on the part of the liver cells to store up its usual percentage of the absorbed sugar, 10 to 20 per cent., by reason of impaired nutrition, disturbance of the portal circulation, or a larger excess of sugar in the blood of the portal vein, it would pass through the liver into the blood of the general circulation and increase the percentage amount of sugar above the normal (0.1 to 0.2 per cent.) establishing the condition of hyperglycemia. This would soon be followed by its elimination from the blood by the kidneys and its appearance in the urine, giving rise to a glycosuria.

In opposition to this view, Dr. Pavy, after years of accurate experimentation, states that the blood on the cardiac side of the liver never under normal circumstances contains a larger percentage of sugar than is to be found in any part of the circulation, except in the portal vein. He states that glycogen is never reconverted into sugar, and denies that the liver produces sugar, to be discharged into the blood; the function of the liver is merely to arrest the passage of sugar, and so to shield the general circulation from an excess; the sugar which arises in the liver after death is a post-mortem product and not an illustration of what takes place during life. Dr. Pavy, having apparently demonstrated the glucosid constitution of protein material in general, accounts for the presence of glycogen in muscles and other tissues on the assumption that during the cleavage of the protein molecule the carbohydrate element is set free and temporarily stored as glycogen. He thus accounts for the production of sugar in the body, even in the absence of all sugar and starch from the food. Pavy believes that the glycogen produced in the liver is utilized in the formation of fat and the synthesis of complex proteins necessary to the construction of the tissues.

The Formation of Urea.—It is now generally believed that the liver is the most active of all the organs which may be engaged in the production of urea. This belief is based on numerous physiologic and pathologic data. The compounds out of which the hepatic cells construct urea have been for chemic reasons asserted to be the ammonium salts, *e.g.*, the carbonate, carbamate, and lactate, which are constantly present in the blood. These salts, which result from protein metabolism, may be absorbed from the tissues or from the intestines, carried to the liver, and there synthesized to urea. This supposition is supported by an experiment as follows: The liver of an animal recently living is removed from the body and its vessels perfused continuously with blood (the urea content of which is known) containing the ammonium salts. An analysis of this blood shows, after a time, a diminution of these salts, and a large increase in the amount of the urea. After the establishment of an Eck fistula (the union of the portal vein with the ascending vena cava whereby the liver is largely excluded from acting on products absorbed from the intestines) there is a marked diminution in the production of urea while the ammonia content of the urine largely increases. One large source for the ammonium which is transformed into urea by the liver cells, is that split off from the protein molecule during digestion by the action of the gastric and pancreatic juices. The ammonia is then absorbed and combined with carbon dioxid with formation of ammonium carbonate. When this compound is transported to the liver by the portal blood, the cells convert it into urea in a manner shown in the following formula:

$$(NH_4)_2CO_3 - 2H_2O = CON_2H_4.$$

Destructive diseases of the liver—*e.g.*, acute yellow atrophy, suppuration, cirrhosis—largely diminish the production of urea, but increase the quantities of the ammonium salts in the urine. The same is true when the liver cells are destroyed during acute phosphorus poisoning.

The Conjugation of Products of Protein Putrefaction.—One of the important functions of the liver is the conversion of toxic compounds, the products of the putrefaction of proteins, into non-toxic compounds. These compounds are formed in the intestine, are absorbed and carried by the blood of the portal vein to the liver. In their passage through the capillaries of the liver they are conjugated for the most part with potassium sulphate by the action of the liver cells and thus deprived of their toxicity. Among the substances thus conjugated are indol, skatol, phenol, and cresol. After absorption indol and skatol are oxidized to indoxyl and skatoxyl and then combined with potassium sulphate giving rise to potassium indoxyl sulphate and potassium skatoxyl sulphate. Phenol and cresol are apparently directly combined with potassium sulphate. All of these compounds then pass into the blood of the general circulation and finally are eliminated by the kidneys. Potassium indoxyl sulphate or indican is the source of the indigo-forming substance found in the urine. Other compounds are likewise reduced in toxicity by the liver cells though the methods by which this is accomplished vary with the nature of the compound. The liver thus presents a chemic defense against the entrance of more or less toxic agents into the blood of the general circulation.

CHAPTER XIX

INTERNAL SECRETION

An internal secretion may be defined as a more or less complex material or agent, produced by the secretor activities of epithelial cells of organs and tissues, and which are discharged into the blood and distributed to organs more or less remote, the activities of which they influence in varying ways and degrees. Some increase, some inhibit physiologic processes while others stimulate growth and in different ways modify metabolism. The internal secretion in many, if not all instances belongs to a class of agents known as *hormones*, agents which according to Starling, are of known or unknown composition, characterized by a relatively simple chemic or molecular composition, an easy diffusibility across the walls of the capillary blood-vessels, a ready susceptibility to oxidation and a rapid elimination, as a result of which, their action does not continue indefinitely.[1]

The internal secretions and the organs by which they are produced, constitute a secondary coördinating mechanism, which supplement the primary coördinating nerve mechanisms of the body; the coöperation of both, however, being necessary for the maintenance of the activities of individual organs as well as of the activities of the body as a whole.

Though the term internal secretion has been applied to various substances such as urea and carbon dioxid, which arise in consequence of tissue metabolism and which, after being discharged into the blood, influence in many ways physiologic processes, yet the term is more applicable to the secretions of organs possessing epithelial cells in anatomic relation to blood-vessels. The glands by which these specific materials or hormones are secreted are known as

Glands of Internal Secretion or Endocrinous Glands.—The glands consist mainly of epithelial cells in close relation to the walls of capillary blood-vessels and lymphatics, and in some instances, if not all, under the control of the central nerve system. By reason of the absence of ducts and their relation to blood-vessels they have also been termed *ductless* glands and *vascular* glands and inasmuch as the secretion is discharged internally (into the blood) they have been designated *endocrinous* glands.

The glands which fall into this category are the thyroid, the parathyroids, the hypophysis cerebri or pituitary, the adrenals, the pancreas, the ovaries. and testicles.

THE THYROID

The thyroid gland or body consists of two lobes situated on the lateral aspect of the upper part of the trachea (Fig. 221). Each lobe is pyriform in shape, the base being directed downward and on a level with the fifth or sixth tracheal ring. The lobe is about 50 mm. in length, 20 mm. in breadth, and 25 mm. in thickness. As a rule, the lobes are united by a narrow band or isthmus of the same tissue. The gland is reddish in color, and abundantly supplied with blood-vessels and lymphatics.

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[1] By reason of the fact that some of the active principles of the internal secretions instead of exciting, relax or inhibit activity, the term hormone for the class is inapplicable according to Schäfer, and he therefore suggests for the latter class, the term 'chalone' from χαλάω, to relax or make slack. Because they act like certain drugs he also proposes the term 'acoid' from '*ákos*, a remedy, to denote this quality, and to denote that they arise within the body, the prefix *aut* can be employed. We thus get the complete expression *autocoid substance* to denote any drug-like principle which is produced in or can be separated from the internally secreting organs and we may divide these autocoid substances into *hormones* or excitatory agents, and *chalones* or inhibitory agents.

Microscopic examination shows that the thyroid consists of an enormous number of closed sacs or vesicles, variable in size, the largest not measuring more than 0.1 mm. in diameter. Each sac is composed of a thin homogenous membrane lined by cuboid epithelium. The interior of the sac in adult life contains a transparent, viscid fluid containing albumin and termed "colloid" substance. Externally, the sacs are surrounded by a plexus of capillary blood-vessels and lymphatics. The individual sacs are united and supported by connective tissue, which forms, in addition, a covering for the entire gland. Nonmedullated nerve fibers derived from the middle and inferior cervical ganglia pass into the gland and are distributed to the walls of the smaller blood-vessels and to the epithelium lining the vesicles (Berkley).

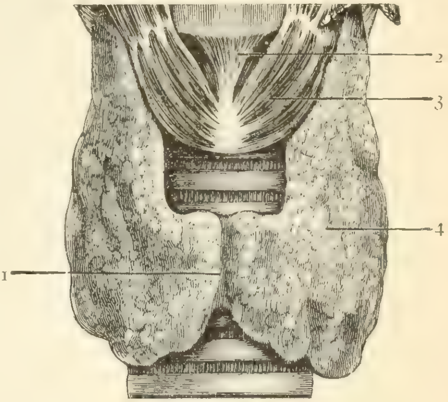

FIG. 221.—VIEW OF THYROID BODY. 1. Thyroid isthmus. 2. Median portion of crico-thyroid membrane. 3. Crico-thyroid muscle. 4. Lateral lobe of thyroid body.—(*After Morris.*)

The rôle played by the thyroid gland and its secretion, especially in mammals in the regulation of the functional activities of various organs and tissues of the body has been determined from the examinanion of the effects that follow its arrested development in the early years of childhood, its degeneration in adults, its surgical removal in human beings when this is necessitated by pathologic conditions, its extirpation in animals, and the ingestion of extracts of the gland or the gland itself.

The Effects of Arrested Development.—A congenital absence of the thyroid or an arrested development in early childhood is followed by a defective physical and mental development characterized by a group of phenomena termed cretinism. The most characteristic of these phenomena are, a small and irregular-shaped body; a swollen face; puffy eyelids; a broad flat nose, a large tongue inclined to hang out of the mouth; a swollen abdomen; short thick legs; mental dullness and stupidity; and even more or less idiocy. The thyroid, as shown on post-mortem examination presents an atrophied appearance and consists mainly of hard fibrous tissue.

The Effects that Follow Degeneration in the Adult.—The degenerative processes that occur in the thyroid in the adult give rise to a group of phenomena the most striking of which is a swollen condition of the skin, the result of the hyperplasia of the subcutaneous connective tissue, of an embryonic type and rich in mucinoid material, to which the term *myxedema* is given. Partly in consequence of this change in the skin, the face becomes broader, swollen and flattened, giving rise to a loss of expression. The features in some instances become coarse and irregular. With the progress of the disease the mind becomes dull and clouded, the memory becomes defective, dementia supervenes and finally the condition of idiocy may be established.

The Effects of Surgical Removal in Man and Animals.—The complete removal of the thyroid gland by surgical procedures necessitated by grave pathologic conditions has been followed in human beings by a serious morbid condition to which the terms *cachexia strumapriva* or *thyroprivia* have been applied. Within a relatively short time the patients complained of muscle fatigue, a sense of heaviness in the limbs and more or less pain. With the progress of the disordered condition there developed a swelling of the face, hands and feet similar to that observed in myxedema. The mental processes became sluggish, the speech difficult and movements slow. A mental condition, approximating idiocy was finally developed before death supervened. With the development of knowledge, regarding the function of the thyroid it was found possible to remove a large portion of the diseased gland without the development of unfortunate results, providing a small portion, sufficiently large, however, to maintain the necessary amount of internal secretion was left behind.

The extirpation of the thyroid in animals is usually fatal though the effects differ according to the animal operated on. Herbivorous animals as a rule survive the removal of the gland far better than carnivorous animals, though no sufficient reason for this difference has been presented. Dogs usually die in a few weeks, death being preceded by tremors, and convulsions. Monkeys, according to Horsley's experiments and observations, generally die within a few weeks. Among the symptoms which developed within a few days after the removal of the gland may be mentioned loss of appetite, fibrillar contractions of muscles; tremors and spasms; mucinoid degeneration of the skin, giving rise to puffiness of the eyelids and face and to a swollen condition of the abdomen; hebetude of mind, frequently terminating in idiocy; fall of blood-pressure; dyspnea; albuminuria; atrophy of the tissues, followed by death of the animal in the course of from five to eight weeks. The complexus of symptoms observed in monkeys was divided by Horsley into three stages: viz., the neurotic, the mucinoid, and the atrophic.

It is evident from the foregoing facts, that the presence of the thyroid is essential to the normal activity of the tissues generally. As to the manner in which it exerts its favorable influence, there is some difference of opinion. The view that the gland removes from the blood certain toxic bodies, rendering them innocuous and thus preserving the body from a species of auto-intoxication, is gradually yielding to the more probable view that the epithelium is engaged in the secretion of a specific material, which finds its way into the blood or lymph and in some unknown way influences favorably tissue metabolism. This view of the function of the thyroid is supported by the fact that successful grafting of a portion of the thyroid beneath the skin or in the abdominal cavity will prevent the usual symptoms which follow thyroidectomy.

The Effects of Feeding the Thyroid Gland.—On the supposition that the thyroid gland secreted and discharged into the blood an agent necessary to the maintenance of the normal metabolism, it was thought probable that the internal administration of the gland or its extracts might provide the body with the necessary amount of the secretion. Acting on the suggestion, fresh thyroids of various animals, principally from sheep, have been administered to myxedematous patients with the result of relieving them of their unfortunate symptoms and of restoring them to a normal physiologic condition. Equally, if not more surprising, are the results which have followed the internal administration of thyroids to cretins. The long-continued treatment changed the entire metabolism resulting in an increase in growth and weight and an awakening of the child's mentality.

Hyperthyroidism.—If the gland extracts are administered in sufficient quantity and for a sufficient length of time when the body is in a normal condition the internal secretion influences very markedly the general metabolism as shown by an increased oxidation of fat and protein and a decline in body weight. If the dosage be large toxic symptoms may arise, *e.g.*, vertigo, increased cardiac action, flushing, tremors, glycosuria, and in monkeys, exophthalmos and a widening of the palpebral fissure. From these facts the inference has been drawn from the clinical side that the symptoms comprised under the term exophthalmic goiter, viz.: rapid action of the heart, pulsation of the large arteries at the base of the neck, protrusion of the eyeballs and fine tremors of the hands are due to an enlargement of the gland and a hypersecretion of the thyroid cells, a condition spoken of as *hyperthyroidism.* This inference has apparently been confirmed by the disappearance of the symptoms after the removal of a large portion of the gland, care being taken to leave a small portion sufficiently large, however, to produce the necessary amount of the internal secretion.

The Thyroid Secretion.—The chemic features of the material secreted and obtained from the structures of the thyroid indicate that it is a complex protein containing iodin, which, under the influence of various reagents, undergoes cleavage, giving rise to a non-protein residue, which carries with it the iodin and phosphorus. The amount of iodin in the thyroid varies from 0.33 to 1 milligram for each gram of tissue. To this compound the term *iodo-thyrin* has been given. The administration of this compound produces effects similar to those which follow the therapeutic administration of the fresh thyroid itself, viz.: a diminution of all myxedematous symptoms. In normal states of the body, iodo-thyrin influences very actively the general metabolism. It gives rise to a decomposition of fats and proteins and to a decline in body-weight. In large doses it may produce toxic symptoms, *e.g.*, increased cardiac action, vertigo, and glycosuria.

The Functions of the Thyroid Gland.—The functions of the thyroid gland which have been drawn from the results that have followed its removal from animals by surgical procedures, have been made questionable, since the discovery of the parathyroid glands and a study of the phenomena which follow when they alone are removed. From their situation and close relationship to the thyroid gland it is generally accepted, that in the earlier experiments, especially those made on cats and dogs, and some other carnivorous animals, both sets of glands were removed and hence some of the symptoms which developed after the removal of the thyroids were due to the loss of function not of the thyroid but of the parathyroids.

This is especially true of the fibrillar contractions, tremors and spasms. These it is now more generally believed arise only in consequence of the simultaneous removal of the parathyroids.

The function or the physiologic action of the thyroid is to produce an internal secretion which after its entrance into the blood promotes favorably the metabolism of the neuro-muscular systems at least. The myxedema and the failure of the mental powers are attributed to the loss or degeneration of the gland and hence its internal secretion, and cretinism to the arrest of its development.

THE PARATHYROIDS

The parathyroids are small bodies, usually four in number, two on each side. They are divided into superior and inferior. The superior are situated internally and on the posterior surface in close relation to, and frequently imbedded in, the substance of the thyroid; the inferior are situated externally, sometimes in contact with, and at other times removed a variable distance from the thyroid (Fig. 222). Microscopically the parathyroids consist of thick cords of epithelial cells separated by septa of fine connective tissue and surrounded by capillary blood-vessels.

Effects of Parathyroid Removal.—The surgical removal of the parathyroids is followed in the course of from two to five days by the death of the animal preceded in most instances by a series of symptoms which are embraced under the general term "tetany." These symptoms are fibrillary contractions of muscles, tremors, spasmodic contractures and paralyses of groups of muscles and not infrequently convulsive seizures and coma. During the convulsion there is an acceleration of the heart-beat, and increase in the respiratory movements which frequently become dyspneic in character. There is also a loss of appetite, nausea, mucous vomiting, and diarrhea. Death may occur during a convulsion or from coma. (Morat and Doyon.) The administration of calcium causes the tetany to disappear and relieves the animal of these various symptoms, from which it is inferred that the parathyroids influence or regulate calcium metabolism.

These results for the most part occur only when all the parathyroids are removed It is asserted that even if one gland is retained the animal does not die. The above described symptoms may manifest themselves, however, but they are slight in degree. Under these circumstances there is a diminished tolerance for sugar as shown by the appearance of sugar in the urine when the normal amount is ingested.

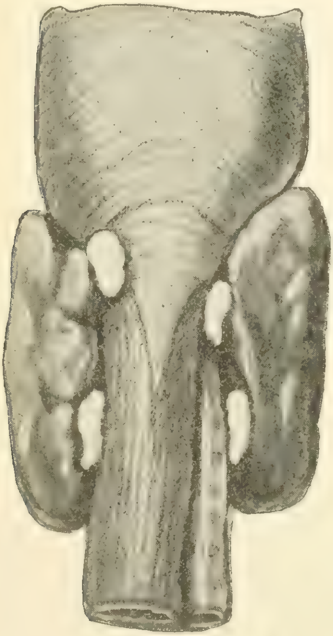

FIG. 222.—The position of the parathyroid glands.—(*Zuckerkandl.*)

Vincent and Jolly have recently published the results of a series of experiments which seem to negative to some extent the preceding statements. These experimenters state that while it is true, that, as a rule, the removal of both thyroids and parathyroids in the carnivora is a fatal operation, there are nevertheless many exceptions; and in the mammalia generally, *e.g.*, cats, dogs, foxes, guinea-pigs, rats, and monkeys, the exception becomes the rule as more than 51 per cent. of animals survived the operation for a prolonged period and of these 68 per cent. showed no specific symptoms of any kind. From the contradictory observations it is evident that the subject needs further investigation.

THE PITUITARY

The pituitary is a small body lodged in the sella turcica of the sphenoid bone. It measures 14 mm. from side to side, 8 mm. from before backward, and 6 mm. from above down, and consists of an anterior lobe somewhat pink in color, and a posterior lobe yellowish-gray in color. The anterior lobe is much the larger and partly embraces the posterior lobe (Fig. 223). The anterior lobe is developed from an invagination of the ectoderm of the buccal cavity and consists of gland tissue surrounded by a thin envelope of connective tissue. It becomes separated from the mouth by the fusion of the sphenoid cartilages. The posterior lobe is an outgrowth from the mid-brain and is connected with the infundibulum of the third ventricle by a short stalk. In the early stages of its development it presents a central cavity which is, however, soon obliterated by the growth of special tissues. It persists in the cat. It has been suggested that the term hypophysis cerebri be reserved for the anterior lobe and the term infundibular body for the posterior lobe. This distinction appears to be desirable inasmuch as in their origin, structure and functions they are separate and distinct bodies.

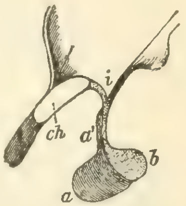

Fig. 223.—Sagittal Section of the Pituitary Body and Infundibulum with Adjoining Part of Third Ventricle. *a.* Anterior lobe. *a'.* A projection from it toward the front of the infundibulum, *b.* Posterior lobe connected by a stalk with the infundibulum, *ch.* Section of optic chiasm.—(*Schwalbe from Quain.*)

Histology of the Pituitary Body.—If a mesial sagittal section be made through the pituitary it will present an appearance which in a general way is the same in many animals though the details vary somewhat in each animal. In the monkey the arrangement of the anatomic parts (Fig. 224) is similar to the arrangement in man. It will be observed that the posterior lobe is solid and that there is no open connection with the cavity of the third ventricle; that it is invested, over a large part of its surface, by a thin layer of epithelium. The anterior lobe, which lies in front of it is separated by a cleft which is the remnant of the cavity of the buccal pouch. Though the appearance of the anterior lobe, and the epithelial investment of the posterior lobe is somewhat different, the latter is but a differentiation of the former, a procedure that takes place in fetal life. The epithelial investment is usually spoken of as the *pars intermedia*, and regarded histologically and physiologically as a part of the posterior lobe. Superiorly the anterior lobe and the pars intermedia are united, though a portion of the latter passes upward and embraces, if it does not entirely surround, the infundibular stalk; inferiorly and posteriorly the two bodies also unite. The posterior surface of the posterior lobe is free from epithelial investment in the mid-line. The extent to which the epithelium invests the posterior lobe varies in different animals. In the cat and dog it is almost complete.

Microscopic examination of the anterior lobe shows the presence of granular epithelial cells, the descendents of the original buccal epithelium, arranged in columns between which pass large thin-walled blood-vessels. In view of the physiologic importance of this lobe it is believed that the granules of the cell represent an internal secretion, which passes into the blood-stream and is thus distributed to various regions of the body.

The pars intermedia consists of several layers of finely granular epithelial cells which develop a colloid material that subsequently passes into the posterior lobe where it becomes hyaline in character. The epithelial investment is separated from the posterior lobe by a layer of blood-vessels though columns of cells penetrate it.

The posterior lobe consists of neuroglia cells and fibers. True nerve-cells are apparently wanting. Throughout the lobe there are numerous small hyaline bodies which are apparently streaming upward to the ventricular cavity. In view of the physiologic importance of this infundibular body or *pars nervosa*, these hyaline masses are believed to represent an internal secretion which passes upward through loose tissue channels toward the infundibulum to be discharged into the fluid of the third ventricle. If the stalk be divided there is an accumulation of these bodies in the posterior lobe. Both parts of the pituitary are well supplied with blood though from different sources.

Effects of Total Removal.—The effects which were observed by the earlier investigators to follow total removal of the hypophysis were not always in accord by reason of the difference in the operative methods pursued, injuries to the brain, infections, imperfect removals as shown by post-mortem examination, etc. Some investigators claimed that after total removal animals lived for long periods and that therefore the gland was not essential to life; others claimed, however, its total removal was followed very shortly by death preceded by a series of characteristic symptoms and that therefore it was absolutely essential to life. The introduction of a new method of procedure for the removal of the hypophysis by Paulesco and its employment by Cushing and his co-workers has led to results which are for the most part in general agreement. This method involves an approach to the gland through the temporal bone instead of through the buccal cavity as was formerly the case. The temporal muscles are first dissected away from the skull on both sides and reflected downward. Large openings are made in the bone and dura of both sides. The temporal lobe on one side is lifted up with a spoon-shaped spatula sufficiently large to expose the hypophysis, hanging from the infundibulum. Owing to the

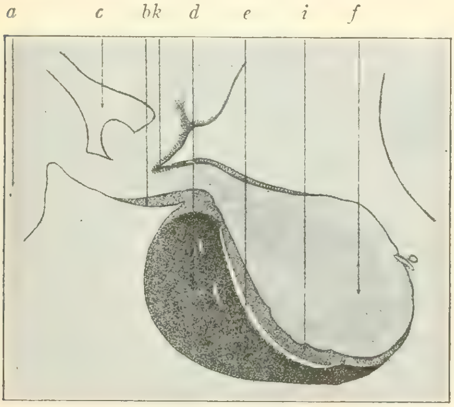

FIG. 224.—MESIAL SAGGITAL SECTION OF THE PITUITARY BODY OF THE MONKEY. *a*, Optic chiasm; *b*, process of the pars intermedia; *c*, third ventricle; *d*, anterior lobe proper; *f*, posterior lobe or pars nervosa; *i*, epithelium investment of the posterior lobe; *k*, epithelium of the pars intermedia passing over the neighboring brain mass; *e*, cleft.—(*After Herring.*)

opposite opening in the skull, the opposite half of the cerebrum is displaced and protruded so that injury to the brain from compression is prevented. The gland can then be picked up with forceps and removed. Paulesco reported that the total removal of the gland in 24 dogs resulted in death in 24 hours. In seven other animals the fatal result was postponed for variable periods. One animal survived for five months and another for a year without exhibiting any very characteristic symptoms. As a post-mortem examination showed that the gland was only partially removed it was assumed that the remaining portion had been sufficient to maintain life. Removal of the *anterior lobe* alone was followed by death as certainly as when the entire gland was removed. Removal of the *posterior lobe* alone was not followed by noticeable effects. From these facts Paulesco asserted that the hypophysis is an organ indispensable to life as its removal rapidly eventuates in death, and that of its different parts the anterior lobe is the more important. Crowe, Cushing and Homans have more recently reported a series of 100 operations for the removal of the hypophysis, the results of which are corroborative in many respects of the results of Paulesco. It was found that the duration of life in adult dogs was from two to three days and in young dogs about eleven days. In a few cases the animals survived for several weeks but a post-mortem examination showed that small viable portions of the gland had escaped removal. Among the many symptoms that followed total hypophysectomy according to these experimenters the more striking after 24 hours were a lowering of body-temperature, unsteadiness of gait and stiffness of movement, a fall of blood-pressure, feeble and slow respiration, muscle twitchings, lethargy, coma, and death. In old animals there was occasional glycosuria; in young animals polyuria. Total removal of the anterior lobe alone in this series of experiments was also as fatal as removal of the entire gland.

The Effects of Partial Removal of the Anterior Lobe.—When only a portion of the anterior lobe was removed the animal survived for a much longer period than when the removal was complete. The duration of life apparently depended on the amount and the cellular activity of the parts left behind. As a result of the partial removal only there developed a series of phenomena to which the term cachexia hypophyseopriva has been given. These phenomena varied somewhat in accordance with the age of the animal. Adult animals became adipose and degenerated sexually, young animals likewise became adipose but they remained undersized and failed to develop sexual characteristics and hence sexual infantilism persisted. The organs of reproduction in both sexes remained rudimentary. The temperature was subnormal and nutritive disorders of the skin developed. These various symptoms were attributed at the time to the partial removal of the anterior lobe alone and hence a deficiency of secretion, but the results of a series of experiments, subsequently published by Cushing, led to the belief that some of these phenomena were due to injury or impairment of the normal function of the posterior lobe at, or subsequent to, the time of the operation. Just which of these phenomena were to be attributed to a diminished secretion of the anterior lobe and which to a diminished secretion of the posterior lobe was left for future experiments to determine. However important the function of the anteror lobe may be in relation to the phenomena just mentioned, it is apparent that it must have some additional function of even greater significance or else its removal would not be attended with fatal results.

The Effects of Pathologic Conditions.—In recent years the idea has gradually developed that certain pathologic states of the body are associated in some way with pathologic states of the pituitary body. Thus the condition of giantism which begins in youth and the condition of acromegaly which appears in adult life are believed to be the result of a hypersecretion of the anterior lobe, which in turn may be due to a hyperplasia of the gland elements excited by a variety of causes. In both giantism and acromegaly there is an increased activity in the nutritive process leading to an overgrowth of osseous tissue and the overlying structures. In the former condition the overgrowth is general; in the latter it is confined to the face and the extremities, hands and feet. To this phase of pituitary activity the term hyperpituitarism has been given.

The opposite condition, infantilism and adiposity, have also been shown to be associated with pathologic changes in the pituitary. In these cases not only is the individual of small size but the genital organs are undeveloped. In addition there may be a subnormal temperature, loss of hair, etc. These phenomena may be due to a diminished or defective secretion partly of the anterior lobe and partly of the posterior lobe. To this condition the term hypopituitarism has been given.

Goetsch has reported recently that the feeding of an extract of the anterior lobe to young rats "has a stimulating effect upon the growth of the animal and upon its sexual development and activity." Infantilism and a want of sexual development may therefore be due to a deficiency of the anterior-lobe secretion early in life.

The Effects of Removal of the Posterior Lobe.—Cushing in a series of experiments (1911) has demonstrated that the posterior lobe with its epithelial investment exerts, contrary to general opinion, a profound influence on metabolism and more especially on the metabolism of the carbohydrates, either alone or in conjunction with other glands having internal secretions. These experiments also led to the belief that some of the phenomena detailed in the foregoing paragraph, especially the deposition of fat, the subnormal temperature and perhaps the imperfect development of the sexual organs are due rather to a deficiency or absence of the secretion of the posterior lobe than to a deficiency or absence of the secretion of the anterior lobe.

It has apparently been demonstrated by Cushing that the hyaline bodies found in the posterior lobe represent an internal secretion; that they are discharged into the cavity of the third ventricle where they undergo solution in the cerebrospinal fluid, by means of which the dissolved material enters the blood-stream, since compression of the infundibular stalk gives rise to an accumulation of the hyaline material. The presence in the cerebrospinal fluid of an agent that produces the same physiologic effects when intravenously injected, as injections of extracts of the posterior lobe do, has also been established.

In the various operative procedures incident to the removal of the entire hypophysis or of the anterior lobe a transient glycosuria is frequently observed, a phenomenon attributed to the discharge under the circumstances of an excessively large amount of the reserve hyaline substance or of the posterior lobe secretion into the cerebrospinal fluid in the third ventricle.

This secretion diminishes temporarily the normal toleration or assimilation of sugar and in some unknown way leads to a hyperglycemia and glycosuria.[1] If the customary amount of sugar is ingested a portion of it will be eliminated in the urine.

If the posterior lobe with its epithelial investment is totally removed or if the infundibular stalk is compressed by a clip so as to prevent the discharge of the secretion into the ventricle the animal becomes very tolerant of sugar and is enabled to assimilate larger quantities than formerly without the development of alimentary glycosuria. As a probable result of the increased carbohydrate assimilation, a condition of nutrition is established, characterized by a general deposition of fat suggesting a conversion of the sugar into fat. There is probably at the same time an imperfect oxidation of the carbohydrates as indicated by the lowered temperature.

That the condition of generalized adiposity is probably due to deficient posterior lobe secretion is shown by the fact that the increased tolerance for sugar can be lowered very promptly by the coincident intravenous or subcutaneous injection of extracts of the posterior lobe.

From the foregoing facts it may be assumed that the secretion of the posterior lobe in some unknown way influences the metabolism of sugar. From the facts at hand it may be assumed that a hypersecretion from any cause whatever, leads to a diminished tolerance for or assimilation of sugar, as shown by the hyperglycemia and glycosuria, though the manner in which the hyperglycemia is developed, whether by a more rapid conversion of glycogen to sugar or by an inefficient storage of sugar as glycogen is unknown. A hyposecretion from any cause leads to an increased tolerance for or assimilation of sugar which eventually contributes to the formation and deposition of fat. In the complexus of symptoms that accompany pathologic changes in the hypophysis either in the anterior or posterior lobe it is difficult to indicate those which are to be attributed to increased or decreased secretion of either the anterior or posterior lobe by reason of their close juxtaposition and their possible simultaneous involvement; again it is also uncertain as to whether the secretions produce their effects alone or through the coöperation of the secretions of other organs having more or less influence in the metabolism of the carbohydrates.

The Effects of Injections of Extracts.—The extracts of the anterior lobe when intravenously injected appear to be without any appreciable effect on any of the physiologic mechanisms. Injections of the extracts of the posterior lobe, however, give rise very promptly, as shown by Howell, to an increase in the blood-pressure which appears to be due to an increased contraction of the arteriole muscle rather than to a stimulation of the vasomotor centers, as the contraction takes place even after destruction of the spinal cord and medulla oblongata. The action of the active constituent of the extract appears to be very general as there is a simultaneous diminution, as shown by plethysmographic investigations, in the volume of various organs. On the heart the extract has an inhibitor action which takes place concomitantly with the contraction of the arterioles and the rise of the pressure as shown by Howell. This is attributed to a direct stimulation of the cardio-inhibitor center as the retardation is partly prevented at least when the vagus is divided or its function suspended by atropin. Even after this has been done, however, a slowing of the heart may still be induced, a fact which suggests that the extract acts directly on the heart-muscle as well. Schäfer and his co-workers have also demonstrated that pituitary extracts cause dilatation of the renal vessels and stimulate specifically the renal cells to activity, thus causing a marked diuresis. The extract also stimulates the non-striated muscles of the intestines, bladder and uterus, giving rise in each instance to vigorous contractions; it also causes a marked discharge of milk from the mammary gland during lactation due to the contraction of the walls of the milk ducts; the dilatator muscle of the iris is also stimulated, causing dilatation of the pupil. A pharmaceutical preparation of the pituitary, "pituitrin", in a similar manner raises the blood-pressure for a considerable period, stimulates intestinal peristalsis and excites contractions of the uterus during and after labor.

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[1] The normal tolerance for cane-sugar in the case of the dog, when it is given by the mouth is about 10 grams per kilo of body-weight and for human beings about 2 grams (glucose) per kilo of body-weight or approximately 150 grams. Any increase beyond this amount appears in the urine indicating that the assimilation limit has been exceeded.

The Functions of the Pituitary or Hypophysis.—The functions of the pituitary body are related to the activities of the anterior and posterior lobes. The anterior lobe, through its internal secretion stimulates the growth of the skeleton and associated tissues as apparently shown by the fact that an excess of secretion in early life leads to giantism and in adult life to acromegalia, while a deficiency of secretion leads to defective growth and the establishment of infantilism. The posterior lobe through its internal secretion assists in the regulation of carbohydrate metabolism as shown by the fact that an excess of secretion lowers the assimilation capacity and thus develops glycosuria, while a deficiency of the secretion raises the assimilation capacity and leads to the production and accumulation of fat.

ADRENAL GLANDS

The adrenal glands or suprarenal capsules are two flattened bodies, somewhat crescentic or triangular in shape, situated each upon the upper extremity of the corresponding kidney, and held in place by connective tissue. They measure about 40 mm. in height, 30 mm. in breadth, and 6 to 8 mm. in thickness. The weight of each is about 4 gm. Accessory glands are sometimes found in the surrounding connective tissue along the abdominal sympathetic and in the neighborhood of the genital organs.

In some animals such as the dog, cat and rabbit, these glands have no anatomic connection with the kidneys, but are situated at varying distances from them.

Histology.—The gland is covered externally by a fibrous tissue from which septa pass into the more central portions thus forming a framework for the support of blood-vessels and cells.

A section of the gland shows just beneath the capsule an outer portion termed the cortex and an inner portion termed the medulla (Fig. 225). The cortex consists mainly of cuboid cells arranged in cylindric columns. The outer layers of cells are arranged in irregular masses forming what has been called the zona glomerulosa. The medulla consists of uniting and interlacing cords of polyhedral cells, the cytoplasm of which contains granular matter and a distinct nucleus. When treated with chromic acid or chromium salts the cytoplasm stains a dull brown or yellow color. For this reason they are termed *chromaffin* cells. Similar cells are found in sympathetic ganglia.

The gland is abundantly supplied with blood-vessels and nerves. The arteries are branches of the aorta, the phrenic, and renal arteries. After penetrating the gland they divide into smaller branches and capillaries which ultimately come into close relation with the cells of both the cortex and medulla. The veins emerge from the gland at the hilum and empty on the right side into the vena cava and on the left side into the renal vein.

The nerves passing to the gland are derived for the most part from the autonomic system. The pre-ganglionic fibers pass from the cord by way of the splanchnics to the semilunar ganglion. The post-ganglionic pass from the semilunar ganglia through its branches direct to the gland. According to Bergmann nerves come from the phrenic and vagus also.

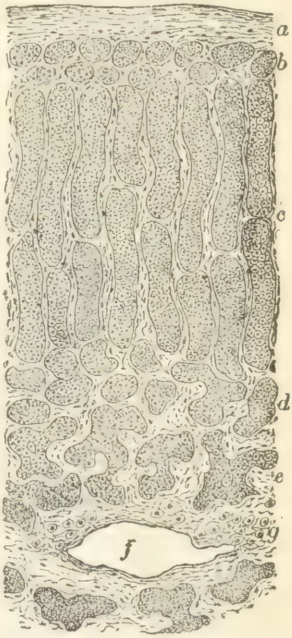

FIG. 225.—SECTION OF HUMAN SUPRARENAL BODY. *a*, fibrous capsule; *b*, zona glomerulosa; *c*, zona fasciculata; *d*, zona reticularis; *e*, medullary cords; *f*, venous channel; *g*, ganglion-cells. (*Piersol*).

Embryologic Development.—Embryologic investigations have shown that the mature adrenal gland consists of two distinct tissues derived from two different portions of the embryo. The cortex is derived from that portion of the mesoderm from which is evolved the precursor of the kidney, the Wolffian body; the medulla is derived from the embryonic sympathetic ganglia and consists primarily of nerve-cells, which, however, in the course of development become profoundly modified. Comparative anatomic studies have shown the relation of these two components of the adrenal body. In the elasmobranch fishes, the shark, ray, etc., the cortex is represented early by an internal body somewhat rod-shaped and elongated and situated toward the posterior portion of the kidney. In the bony fishes this organ becomes paired. The medulla is represented by a series of paired bodies extending along the vertebral column and in close relation to the sympathetic ganglia and contain a number of chromaffin cells. These two elements unite to form the compound adrenal. In the mammals the larger portion of this chromaffin material fuses and becomes enveloped on each side by the internal body with the formation of the existing adrenal body. The unincorporated portions of the chromaffin bodies remain as masses of varying size, found in connection with the sympathetic nerve system. The most important of these bodies is the "abdominal chromaffin body" extending along the aorta from the level of the adrenals to the bifurcation. It is readily exposed in the dog by staining with a solution of bichromate of potassium. Accessory adrenal bodies may consist of either cortical or chromaffin material alone or of both.

The Effects of Disease and Removal of the Adrenal Glands.—There is a profound disturbance of the nutrition first described by Addison and subsequently termed by Trousseau, Addison's disease, which is characterized by extreme muscular weakness and an incapacity for sustained muscle activity; a bronze-like discoloration of the skin and mucous membranes, disturbance of the digestive functions, indicated by indigestion, vomiting and diarrhea; a feeble action of the heart; a small feeble pulse; a low blood-pressure; a subnormal temperature and a feeble respiration. This condition, which is thus largely characterized by a loss of tone in the skeletal as well as the vascular musculature, terminates fatally from a paralysis of the respiratory muscles. Post-mortem examination reveals in all cases a more or less extensive disease of one or both adrenals. A very common lesion is a tubercular degeneration. These symptoms were attributed by Addison to a loss of function of the glands.

The removal of these bodies from various animals by surgical procedures is invariably and in a short time followed by death, preceded by some of the symptoms characteristic of Addison's disease. Thus, shortly after their removal the animal becomes tranquil and apathetic; the respiration soon becomes feeble and difficult; prostration supervenes and the animal appears as though paralyzed, but the irritability of the skeletal muscles and nerves is normal; the heart becomes slow, feeble and irregular; the blood-pressure falls promptly 20 to 30 mm. of mercury, after which it steadily falls to a low level; the appetite fails, the temperature declines and death occurs in from twelve to forty-eight hours. In some instances a pigmentation of the skin similar to that seen in Addison's disease has been observed. From the fact that animals so promptly die after extirpation of these bodies, and the further fact that the blood of some animals is toxic to the subjects of recent extirpation, but not to normal animals, the conclusion was drawn that the function of the adrenal bodies is to remove from the blood some toxic product of muscle metabolism. Its accumulation after extirpation was supposed to cause death through autointoxication. This view is, however, not generally accepted.

The Effects of the Injection of Gland Extracts.—On the supposition that the adrenals might secrete and pour into the blood a specific material that favorably influences general metabolism, Schäfer and Oliver injected hypodermatically glycerin and water extracts of the medulla into the bodies of various animals and observed at once an increased rate of the heart-beats and of the respiratory movements. The effects however were only transitory. When these extracts were injected into the veins directly, there followed in a short time a cessation of the auricular contraction though the ventricular contraction continued vigorously but with a slower rhythm. The blood-pressure at the same time was markedly increased. If the vagi were cut previous to the injection or if the inhibitor influence of the vagi was removed by an injection of atropin the reverse effects were produced, viz., an increase in the rapidity and vigor of both the auricular and ventricular contraction accompanied by a still more marked rise of blood-pressure. This latter effect is the result partly of the increased action of the heart but very largely the result of a vigorous contraction of the muscle-fibers in the walls of the arterioles. This is attributed to a direct stimulation of the arterioles and not to a stimulation of the vaso-constrictor center. The contraction of the arterioles is quite general as shown by plethysmographic studies of the limbs, the spleen, kidney, etc. The arterioles of the lungs and brain do not contract under its influence to the same extent as do the arterioles in other regions of the body, possibly for the reason that the arteriole muscles in these organs are not so abundantly supplied with vaso-motor nerves as they are in other regions of the body. Applied locally to the mucous membranes, adrenalin extract produces contraction of the blood-vessels as shown by the pallor which follows. The skeletal muscles are affected by the extract very much as they are by veratrin. The duration of a single contraction is very much prolonged, especially in the phase of relaxation or of decreasing energy. In the foregoing instances the extract apparently produces its effects by an augmentation of the normal tonus of the arteriole muscle. The effects follow the injection of an extract of the medulla only. An extract of the cortex appears to be without influence.

The injection of small doses of the active principle of the gland into the peritoneal cavity or into the blood is also followed by glycosuria in the course of an hour which may last for several hours.

The Internal Secretion.—It is apparent from the results of these experiments that the adrenal bodies are engaged in elaborating and pouring into the blood a specific material which on the one hand stimulates to increased activity the muscle-fibers of the heart and arteries, thus assisting in maintaining the normal blood-pressure, and on the other hand maintaining the tonicity of the skeletal muscles. An alkaloidal substance was isolated by Abel from extracts of this gland, to which the term *epinephrin* was given. A crystallizable substance was isolated first by Takamine and later by Aldrich, to which the term *adrenalin* was given. Both substances are apparently equally efficacious in causing contraction of the blood-vessels and in raising the blood-pressure. Epinephrin or adrenalin represents the active principle of the gland and is regarded as a product of the secretor activity of the cells composing the medulla. As the effects following the intravenous injection of adrenalin are of short duration, the supposition is that it is speedily oxidized. It is regarded as the typical hormone.

The action of adrenal extract however is not limited to the non-striated muscle-fibers of the arterioles but extends itself to the non-striated fibers found in the the walls of the viscera, *e.g.*, stomach and intestines, gall-bladder, urinary bladder, uterus, etc. The administration of this secretion is followed however, in these regions, by an inhibition of the tonus and subsequent relaxation of the visceral walls, with the exception of the uterus. In the case of the isolated virgin uterus of many mammals, adrenal augments the tone and the vigor of the spontaneous contractions. In addition to the foregoing phenomena, dilatation of the pupil, increased flow of saliva and glycosuria have been observed.

From an examination of the effects that follow the intravenous injection of adrenalin or adrenal extracts, it is apparent that they closely resemble the effects that follow stimulation of the sympathetic nerve in a large part if not in all parts, of its distribution.

It has been a subject of discussion as to whether adrenalin acts on the muscle-fiber directly or upon the endings of the sympathetic nerves with which they are functionally associated. By reason of the fact that non-striated muscles that have no connections with the sympathetic nerve system, are not influenced by adrenalin; and the further fact that non-striated muscles that have been deprived of their nerve connections through degenerative changes following division of the nerves, are influenced by adrenalin, have led to the assumption that it acts neither on muscle nor nerve, but on some material which intervenes between the nerve endings and the muscle but which is intimately related to the muscle. To this material Langley has applied the term "receptive substance." In all instances the adrenalin stimulates the receptive substances as a result of which the normal effect produced by the sympathetic nerve impulse is intensified.

The Influence of the Nerve System.—The secretory activity of the adrenals is regulated by the nerve system. Thus Dreyer found that the blood of the adrenal vein after stimulation of the splanchnics was capable of causing to a much greater extent the usual physiologic effects when injected into an animal than blood of the adrenal vein before stimulation and this independent of the vascular changes that were simultaneously provoked. It has also been shown by Ascher that a high blood-pressure can be maintained by prolonged stimulation of the splanchnics. Cannon has reported that major emotional disturbances such as fright lead to an increase in the secretion of the adrenals as shown by the fact that the blood taken from the vena cava above the level of the adrenal veins will promptly produce an inhibition of a contracting intestinal strip, while blood taken from the animal previous to the fright, had no such effect. After ligation of the veins or the removal of the adrenals there was a failure of this effect upon excitement.

Emotional excitement in cats at least is also attended with hyperglycemia and glycosuria which is probably due to an increase of the adrenal secretion in the blood inasmuch as a similar effect follows the injection of the extract into the blood. The hyperglycemia and glycosuria caused either by the intravenous injection of the extract or by an increased activity of the adrenals following emotional excitement, fear or rage, is difficult of explanation. It may be the result of a direct action or an indirect action through secretor nerves on the liver cells, in consequence of which the stored glycogen is rapidly transformed into sugar and discharged into the blood.

An advantage that would accrue to the animal from the accumulation of sugar in the blood under these circumstances, would be a quickly available source of energy-yielding material, for the continued muscle activity that would attend either flight or defense.

The Function of the Adrenal Gland.—The function of the adrenal gland, at least of the medullary portion, is to furnish an internal secretion which serves apparently to stimulate the receptive substance at the myoneural junction and thus coöperates with the sympathetic system to maintain that degree of frequency and force of the heart-beat and the contraction of the arteriole muscle necessary to maintain the normal blood-pressure; to inhibit as occasion requires, the tonus of muscle walls of various viscera; to cause a mobilization of sugar in the blood when this is necessary, and to increase in some unexplained way the tonus and activity of the skeletal musculature.

The Chromaphil Tissue.—The chromaphil tissue lying along the aorta and in other situations as well—that portion of the original embryonic chromaphil tissue that was not incorporated in the medulla of the adrenal gland—has been shown to possess physiologic actions similar to, if not identical with extracts of the adrenal medulla itself. Thus it causes not only a marked rise of blood-pressure but, according to the recent investigations of Fulk and Macleod, in many mammals it inhibits the spontaneous contractions of isolated intestinal muscle and augments the tone and contractions of the isolated virgin uterus.

The Pancreas.—The pancreas though engaged in the production of an external secretion is yet, by reason of the specialized group of cells, the islands of Langerhans, to be regarded as an organ of an internal secretion as well. These islands it is generally believed are engaged in the secretion of an agent which after entering the blood is carried to the muscles where it activates or assists a glycolytic enzyme in promoting the oxidation of sugar; or it may inhibit normally the stimulating action of adrenalin on the liver cells and thus prevent an excessive output of sugar and the development of hyperglycemia (see page 519). If the entire pancreas is extirpated and the animal survive the operation, a glycosuria is soon established, followed by a series of symptoms resembling those observed in diabetes mellitus as it occurs in man, viz.: thirst, polyuria, loss of energy, decline in body-weight, etc., followed by death in a few weeks. Pathologic processes that involve a large portion of the pancreas likewise give rise to a similar series of phenomena, as ligation of the pancreatic duct, a procedure that leads to a destruction of all portions of the pancreas except the islands of Langerhans and without developing glycosuria has led to the inference that these islands are the agents engaged in the production of the internal secretion.

The Testicles and Ovaries.—The testicles and ovaries are regarded at the present time as glands for the production of an internal secretion, as well as for the production of the characteristic reproductive elements. The testicles possess in the epithelial cells lining the peripheral portions of the seminiferous tubules an apparatus for the development of spermatozoa, and in the cells in the connective tissue between the tubules—the so-called interstitial cells—an apparatus for the production of the internal secretion which is discharged into the blood, and favorably influences the development of the secondary sexual characters, as well as the body as a whole. This general view is based on facts such as the following:

The removal of the testicles early in life and before the age of puberty leads to imperfect development of the vesiculæ seminales and the prostate gland; in addition to these defects, there is a failure of development of the various and distinctly sexual characters peculiar to man and other animals as well. Sexual desire is wanting and the body frequently remains in the infantile state. In some instances, however, there is an increase in the bones of the skeleton and hence the animal increases in size. It has been suggested that the internal secretion controls the growth of the bones by antagonizing the action of some other agent, as the secretion of the anterior lobe of the pituitary, which promotes the growth of the skeleton. That these results are not due to the loss of the structures producing the sperm elements, is shown by the fact that ligation of the vas deferens only, while destroying these structures, does not interfere with development of the sexual characters. Transplantation of the testicles, in cocks and in certain of the smaller mammals that have been castrated, has led to the development of secondary sexual characters which in no apparent way differed from those of control animals. In old age the testicles undergo degenerative changes characterized by a decline in physical vigor, inactivity and a cessation of sexual activity. From the foregoing facts it is apparent that these organs are engaged in the production of an internal secretion which influences favorably the growth, development, and general vigor of the entire body.

Extracts of the testicles have been prepared and injected into the body in advanced years, with a view of reestablishing the former condition of body vigor. Experiments of this character were made originally by Brown-Séquard on himself and reported that his general health, his muscular power and mental activity were much improved. These results have not received general confirmation.

The ovaries are also regarded as glands for the production of an internal secretion, as well as for the production of characteristic reproductive elements. The ovary possesses in the epithelium of the Graafian follicles an apparatus for the development of the ova, and in the cells of the intervening stroma—the so-called interstitial cells—an apparatus for the production of an internal secretion which is poured into the blood and influences not only the development of sexual organs but influences favorably the development of the secondary sexual characters as well as the body as a whole.

The removal of the ovaries of human beings early in life is an operation that is not often performed and hence it is difficult to state the results that might arise. Their removal in certain animals leads to an atrophy of the uterus, and in addition, to a failure of development of secondary sexual characters. Menstruation does not occur and the body does not reach maturity. The removal of the ovaries in adult life results in a cessation of menstruation, and the appearance of a variety of disorders of a body and mental character. Similar phenomena are frequently observed at the menopause, when the ovaries undergo degenerative changes. The administration of extracts of the ovaries—oophorin tablets—is claimed to relieve some of the symptoms following the removal of the ovaries or occurring during the menopause. The transplantation of an ovary into the wall of the uterus or into the broad ligament after ovariotomy in women has, even after the lapse of two years, reestablished menstruation and awakened sexual desire. From facts such as the foregoing it has come to be believed that ovaries also produce an internal secretion which has a marked influence on the body and mental states of women and mammals generally.

THE SPLEEN

The spleen is a soft bluish-red organ, oval in shape, from twelve to fifteen centimeters long by eight broad and four thick. It is situated in the left hypochondrium between the stomach and the diaphragm. In this situation it is held in position by a fold of the peritoneum which passes from the upper border to the diaphragm.

Structure.—A section of the spleen shows that it consists of connective tissue, blood-vessels, lymph-corpuscles, and lymphoid tissue. The surface of the spleen is covered by a capsule composed of dense fibrous tissue, from the inner surface of which septa or trabeculæ pass inward toward the center of the organ. In their course they give off a series of processes which unite freely, forming a spongy connective-tissue framework. The capsule and the main trabeculæ in some animals contain numerous non-striated muscle-fibers. In man they are relatively few in number. The blood-vessels which enter the spleen are supported by the connective-tissue septa. As they pass toward the center of the organ they divide very rapidly and soon diminish in size. In their course small branches are given off, which penetrate the inter-trabecular tissue and become encased with spheric or cylindric masses of adenoid tissue known as Malpighian corpuscles. These corpuscles are composed largely of leukocytes. In some animals the leukocytes, instead of being arranged in masses, are distributed along the walls of the artery as a continuous layer. Within the corpuscles the arteries pass into capillaries; whether the artery passes directly to the splenic pulp or indirectly by way of the corpuscles, its ultimate branches terminate in capillaries which open into the spaces of the splenic pulp. From these spaces a network of venules gathers the blood and transmits it to the veins. It is a disputed question as to whether the spaces are lined by epithelium, thus forming a continuous blood channel, or whether they are wanting in this histologic element.

The Splenic Pulp.—The spaces of the connective-tissue framework are filled with a dark red semifluid mass known as the splenic pulp. When microscopically examined, the pulp presents a fine loose network of adenoid tissue, large numbers of leukocytes or lymph-corpuscles, red corpuscles in various stages of disintegration, and pigment granules. Chemic analysis reveals the presence of a number of nitrogen-holding bodies, *e.g.*, leucin, tyrosin, xanthin, uric acid; organic acids, *e.g.*, acetic, lactic, succinic acids; pigments containing iron, and inorganic salts.

The Functions of the Spleen.—Notwithstanding all the experiments which have been made to determine the functions of the spleen, it cannot be said that any very definite results have been obtained. The fact that the spleen can be removed from the body of an animal without appreciably interfering with the normal metabolism would indicate that its function is not very important. The chief changes observed after such a procedure are an enlargement of the lymphatic glands and an increase in the activity of the red marrow of the bones. The presence of large numbers of leukocytes in the splenic pulp and in the blood of the splenic vein suggested the idea that the spleen is engaged in the production of leukocytes, and to this extent contributes to the formation of blood. The presence of disintegrated red blood-corpuscles has suggested the view that the spleen exerts a destructive action on functionally useless red corpuscles. These and other theories as to splenic functions have been offered by different observers, but all are lacking positive confirmation.

Volume Variations of the Spleen.—It was shown some years since by Roy, with the aid of the plethysmograph, that the spleen undergoes rhythmic variations in volume from moment to moment. In the cat and in the dog the diminution in the volume (the systole) and the increase in volume (the diastole) together occupied about one minute.

This fact was determined by withdrawing the spleen through an opening in the abdominal wall and enclosing it in a box with rigid walls, the interior of which was connected with a piston recording apparatus. The system being filled with oil, each variation in volume was attended by a to-and-fro displacement and a corresponding movement of the recording lever. The special form of plethysmograph used for this purpose is known as the oncometer or bulk measurer, and the recording apparatus as the oncograph.

The cause of these variations in volume Roy attributed to a rhythmic contractility of the non-striated muscle-fibers in the capsule and trabeculæ, and not to changes in the arterial blood-pressure, as the curve of the pressure taken simultaneously remained practically uniform. The effect of the rhythmic contractions of the splenic muscle-tissue is to force the blood through the organ, a condition necessitated perhaps by the pressure relations within, though what function is thereby fulfilled is not apparent.

It was subsequently shown by Schäfer and Moore that the splenic volume is extremely responsive to all fluctuations of the arterial blood-pressure; that though the spleen may passively expand and recoil in response to the rise and fall of the blood-pressure, nevertheless the reverse conditions may obtain: viz., that the splenic volume may diminish as the pressure rises, if the splenic arterioles contract simultaneously with the contraction of the arterioles generally. On the contrary, the splenic volume increase is coincident with a dilatation of the splenic and systemic arterioles. In addition to the rhythmic variations, the spleen steadily increases in volume for a period of five hours after digestion, and then gradually returns to its former condition.

Influence of the Nerve System.—The nerves which supply the vascular and visceral muscles in the spleen are derived directly from the semilunar ganglion (post-ganglionic fibers) and pass to it in company with the splenic artery. The nerve-cells from which they arise are in physiologic relation with nerve-fibers (pre-ganglionic fibers) which emerge from the spinal cord in the anterior roots of the third thoracic to the first lumbar nerves inclusive, though they are found most abundantly in the sixth, seventh, and eighth thoracic nerves. Their center of origin is in the medulla oblongata.

Stimulation of the nerves in any part of their course gives rise to a diminution in splenic volume; division of the nerves is followed by an increase in the volume. In asphyxia the spleen is small and contracted, a condition attributed to a stimulation of the centers in the medulla by the venosity of the blood.

The musculature of the spleen may also be excited to contraction by reflex influences, as shown by the fact that stimulation of the central end of a nerve is attended by a diminution of volume.

Inasmuch as the excised spleen will continue to exhibit variations in volume when perfused with blood, it would appear that it possesses some contractile mechanism independent to some extent of the nerve system.

CHAPTER XX

METABOLISM

It will be recalled that each cell in the body in the living state is the seat of a series of chemic changes which vary in degree from moment to moment in accordance with the degree of functional activity, and on the continuance of which all life phenomena depend. Some of these chemic changes are related to or connected with the molecules of the living material, while others are connected with the food material supplied to them. Of the chemic changes occurring within the molecules some are destructive, dissimilative or disintegrative in character, whereby the molecule is in part eventually reduced through a series of descending chemic stages to simpler compounds which, apparently of no use in the cell, are eliminated from it. It is, therefore, said that the living material undergoes molecular disintegration as a result of functional activity. To these changes the term *katabolism* is also applied. Other of these changes are constructive, assimilative or integrative in character, whereby a part at least of the food material furnished by the blood-plasma is transformed through a series of ascending chemic stages into living material, and whereby it is repaired and its former physiologic condition restored. It is, therefore, said that the living material undergoes molecular integration as a preparation for functional activity. To these changes the term *anabolism* is also applied.

Living material has also a temperature varying in degree in different species of animals as well as in different parts of the same animal. Here as elsewhere the temperature is due to heat liberated from organic compounds through disruption and subsequent oxidation to simpler compounds. Though some of the heat liberated may come from the tissue molecules, the larger part by far comes from the food molecules—sugar, fat, and protein,—constituents of the fluids permeating the interstices of the living material. These foods carry into the body potential energy, ultimately derived from the sun. When they are disrupted and oxidized the potential energy is transformed into kinetic energy which manifests itself for the most part as heat. To the sum total of all the chemic changes occurring in tissues and foods the term *metabolism* is given.

Though the foregoing statements are applied to the individual cell they are equally applicable to the body as a whole, inasmuch as the organs and tissues of which it consists are composed of cells. The body grows in size and maintains its nutrition, by the introduction of food materials which are utilized in part, for the repair of the tissues which have undergone molecular disintegration in consequence of activity, and in part for the liberation of energy. As a result of the disintegration or the metabolism of tissue and food materials, products such as carbon dioxid, urea, etc., are formed which, apparently of no further use, are discharged from the body by eliminating organs as the kidney, lungs, skin, etc. Assimilation and dissimilation are constantly taking place. If the food assimilated and metabolized exactly replaces the tissues dissimilated and the food metabolized the body will retain a condition of nutritive equilibrium.

The term metabolism may, therefore, be applied to the chemic changes which materials undergo, under the influence of living cells. It comprises (1) the elaboration of substances of relatively low composition into substances of higher and more complex composition—anabolism; and (2) their subsequent reduction to substances of lower and less complex composition, as well as the reduction of the relatively less complex food materials —katabolism.

For many reasons it is desirable to know, as far as this is possible the extent and character of the tissue changes, as well as the successive chemic changes which the food materials undergo in their transit through the body from day to day.

In order to obtain this information it is necessary to place the subject of the experiment under conditions which permit of the collection of the excretions for purposes of analysis, and then to deduce from the nitrogen and carbon they contain, the amounts of the tissue materials metabolized in the absence of food; or the amounts of the food materials metabolized when the ordinary amounts of food are consumed. Supplementary facts from the field of physiologic chemistry throw much light on many of the intermediate chemic stages.

The methods by which a metabolism experiment is conducted have been detailed on pages 118–120.

In various sections of the preceding pages some of the facts pertaining to the metabolism of the body have been presented and considered, and it will suffice in this connection to summarize some of the facts already alluded to and to add others not heretofore mentioned.

Before considering the metabolism of the individual organic food materials as it unfolds itself in the animal body under physiologic conditions, it is of advantage to consider the metabolism of living material as it manifests itself when the animal or the human being is deprived of food for a variable length of time or during the starvation process.

THE METABOLISM OF LIVING MATERIAL DURING STARVATION

When an animal is subjected to the conditions of a metabolism experiment and deprived of all food except water and oxygen, it is a relatively simple matter to collect the excretions, to analyze them for nitrogen and carbon and then to calculate from the amounts of each the amounts of protein and fat metabolized from day to day. The carbohydrates may be left out of consideration in a prolonged experiment. The following experiment is illustrative. The man fasted five days and performed light work in the respiration chamber.

METABOLISM OF J. A. IN STARVATION

Day of fasting	N elimination			C elimination			
	Urine	Feces	Total	Urine	Feces	Respiration	Total
1	12.04	0.13	12.17	8.0	1.1	188.5	197.6
2	12.72	0.13	12.84	8.3	1.1	179.4	188.8
3	13.48	0.13	13.61	9.9	1.1	172.2	183.2
4	13.56	0.13	13.69	10.3	1.1	169.4	180.8
5	11.34	0.13	11.47	9.3	1.1	165.8	176.2

From the foregoing figures the following table of the general metabolism is made:

Day of fasting	Protein	Fat	Calories from protein	Calories from fat	Calories, total
1	76.1	206.1	303.5	1916.9	2220.4
2	80.3	191.6	320.5	1781.9	2102.4
3	85.1	181.2	339.4	1684.7	2024.1
4	85.6	177.6	341.4	1651.9	1992.3
5	71.7	181.2	286.1	1684.7	1970.8

—From Lusk's "Nutrition."

From the foregoing table it will be readily observed that with each succeeding day there was metabolized as the result of activity and for purposes of heat-production a certain quantity of protein and fat which on the fifth day amounted to 71.7 grams and 181.2[1] grams, respectively, yielding together 1970.8 Calories.

In prolonged starvation the metabolism of protein and fat continues though in diminishing amounts until both reach the minimum just previous to death, which for the protein is about 18 or 20 grams. The minimum for the fat at this period depends on the amount of fat in the body prior to the starvation period.

During the course of the starvation there is a corresponding decline in the body weight. Coincidently certain disorders of nutrition arise. (For further particulars regarding starvation metabolism, the loss of weight of different tissues and the post-mortem appearance the reader is referred to pages 128 and 129.)

THE METABOLISM OF THE BODY ON A MIXED DIET

As an illustration of the result of a metabolism experiment on a mixed diet the following experiment of Pettenkofer and Voit may be cited. The subject was a man, weighing 70 kilograms and at rest.

On a mixed diet the materials under outcome were collected; from their amounts it was calculated that the body had received the amounts of the food principles under income.

COMPARISON OF THE INCOME AND OUTCOME

Income			Outcome			
	N in grams	C in grams		N in grams	C in grams	H_2O in grams
137 grams albumin...... 117 grams fat.......... 352 grams carbohydrate.. 2016 grams water........	19.5	315.5	Urine......	17.4	12.7	1279
			Feces......	2.1	14.5	83
			Exp. air............		248.6	828
				19.5	275.8	2190

It will be observed that the body was in nitrogenous equilibrium; that it stored up 39.7 grams of carbon equivalent to 52 grams of fat, and that it eliminated 174 more grams of water than were consumed.

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[1] The fat is calculated from the carbon remaining after deducting the carbon derived from the protein which is equal to 3.28 grams for each gram of nitrogen eliminated.

THE METABOLISM OF THE PROTEINS

It will be recalled that the protein constituents of the food introduced into the alimentary canal are reduced by the action of the enzymes of the gastric and pancreatic juices to relatively simple compounds, viz.: ammonia, amino- and diamino-acids which are for the most part at once absorbed into the blood. A portion of the ammonia and a portion of some of the amino-acids pass into the large intestine where they give rise under the destructive action of bacteria to substances of a simpler character such as indol, skatol, and phenol. These and other putrefactive substances are in part discharged from the body in the feces and in part absorbed into the blood and ultimately eliminated in combination with potassium sulphate by the kidney (see pages 458 and 488). The ammonia absorbed is converted during its passage through the liver into urea.

The absorbed amino-acids, after passing through the liver and gaining entrance into the general circulation, are distributed to the tissues where they are in part utilized for the reconstruction of the tissue molecules that have undergone metabolism in consequence of their functional activity, and in part separated by the action of tissue enzymes into the amine element NH_2, and a carbonaceous radical. The percentage of the amino-acids used for the former purpose varies at different periods of life and under varying circumstances. In youth when tissues are developing and growing and at the same time are undergoing an active metabolism, a larger percentage is utilized for repair and growth than in adult life when the body-growth at least has ceased, though metabolism continues more or less actively.

The amine element, NH_2, and the carbonaceous radical arising from the cleavage of the amino-acids not utilized for tissue growth and repair are disposed of as follows. The NH_2 is combined with hydrogen and then with CO_2 to form ammonium carbonate which, perhaps in the tissues, certainly in the liver is transformed into urea; the carbonaceous radical is oxidized to CO_2 and water with the liberation of heat. The heat-producing power of protein—4 Calories per gram—is almost entirely due to this oxidation. Since scarcely more than half the protein consumed is utilized for tissue repair the question has been raised as to whether a smaller amount than that usually consumed viz.: 100 to 120 grams, would not be equally satisfactory. For statements regarding the advantages of a low- and high-protein diet see pages 121 and 122.

The tissue protein, sooner or later, also undergoes katabolism in consequence of functional activity, and the natural supposition would be that it too is reduced to its constituent amino-acids which are then disposed of by the methods already alluded to. Nevertheless there are reasons for thinking that this is not wholly the case. Folin has presented a series of facts that lead to the supposition that this portion of the protein is represented in part by creatinin. Thus it has been shown that while the urea excreted rises and falls with the protein consumed, the amount of creatinin excreted remains more or less stationary; again, in individuals of pronounced muscle development, after unusual muscle activity and in diseases involving a destruction of muscle-tissue there is an increase in creatinin elimination. In the opposite conditions the amount excreted is low. For these and other reasons creatinin is regarded as a specific final end-product and an indicator of the metabolism of muscle protein.

The Metabolism of the Nucleo-proteins.—The tissue cells of animal and many vegetable foods contain nuclei into the composition of which nucleo-proteins enter. In the metabolism of the nucleo-proteins it is assumed on the basis of their reaction with hydrolyzing agents that they undergo a cleavage into a protein and nuclein. The nuclein subsequently gives rise to nucleic acid which, under the influence of an enzyme, is separated into two bases, guanin and adenin; these bases under the action of two enzymes, *guanase* and *adenase*, are combined with water, deaminized and transformed into xanthin and hypoxanthin. The oxidation of these latter compounds gives rise to uric acid. (See page 13 and 457.)

THE METABOLISM OF THE FAT

It will be recalled that during the digestive process the neutral fats are gradually reduced by the action of the enzyme lipase of the pancreatic juice to corresponding fat acids and glycerin; that subsequently the fat acids combine with alkalis to form soaps, after which both soaps and glycerin are absorbed. After absorption and during their passage through the epithelial cells covering the villi, the soap and glycerin are synthesized into fat globules and deposited in the cell material. Subsequently the fat granules enter the lymph-vessels of the mesentery and by which they are discharged into the thoracic duct and finally into the blood at the junction of the subclavian and internal jugular veins. After a meal rich in fat, the amount of fat in the blood may be so great as to impart to it a distinctly pink color. In the course of several hours the fat disappears. As to the change it undergoes before it passes across the capillary wall there is much obscurity. It is stated by Hanriot, that a lipase in blood again hydrolizes the fat to fat acids and glycerin and in consequence of their solubility, pass out into the lymph-spaces. By ultra-microscopic methods of illumination the fat may be observed as "blood dust," in vigorous Brownian movement (Bayliss). It is possible that under this form they pass into the lymph-spaces. As to the final disposition of the fat the general belief is, that when it is consumed in normal amounts and under physiologic conditions it promptly undergoes oxidation in the tissue cells yielding carbon dioxid and water with the liberation of heat.

The intermediate stages through which fat passes have not been wholly determined. Nevertheless it is a well-founded supposition that the first stage is a cleavage of the neutral fats to fat acids—stearic, palmitic and oleic, and glycerin.

These fat acids are the higher members of the fat acids and are characterized by a high molecular weight. Before they can undergo complete oxidation they must be reduced to lower acids of the fat acid series, acids of a low molecular weight.

This is accomplished presumably by successive cleavages and oxidations. Thus stearic acid which consists of 18 carbon groups is successively reduced by oxidation of the carbon atom in the beta position until the four carbon stage is reached when the resulting acid is known as butyric acid, *e.g.*, $CH_3.CH_2.CH_2.COOH$. Upon oxidation of the beta carbon atom there is formed β-oxybutyric acid, viz.: $CH_3.CHOH.CH_2.COOH$.

The succeeding oxidation results in the removal of the two hydrogen atoms attached to the beta carbon atom and results in the formation of aceto-acetic acid or diacetic acid, viz.: $CH_3.CO.CH_2.COOH$, which by the loss of a molecule of CO_2 yields acetone, viz.: $CH_3.CO.CH_3$.

Acetone by a further oxidation is converted into carbon-dioxid and water. Thus by these successive oxidations the stored-up energy of the fat is liberated as heat.

If fat is consumed in too large a quantity the last stage may not be wholly completed and some of the acetone produced may be eliminated in the urine. Analysis of the urine generally shows the presence of acetone to the extent of 0.01 to 0.03 grams daily.

In diabetes these three compounds—β-oxybutyric acid, aceto-acetic acid and acetone—make their appearance in the urine. Since all oxidations are preceded by a cleavage the inference is that in this disease there is an absence of the enzyme necessary to effect the cleavage of the oxybutyric acid and thus permit of further oxidation. The accumulation of this acid in the body establishes the condition known as *acidosis* and in turn to coma and death.

The Origin of the Body Fat.—1. *From Protein.*—It is a familiar observation that on the customary diet the animal body frequently accumulates a large amount of fat. The question, therefore, has arisen as to its origin, and many experiments have been made to determine it. If an animal is placed on a protein diet, fat is very seldom deposited. If the protein is consumed in normal amounts, and the fats and carbohydrates in excess of the normal amounts, there is generally an accumulation and storage of fat. It was for a long time taught by v. Voit that the carbonaceous radical set free in the metabolism of protein was retained in the body and deposited as fat. This origin of fat has largely been disproven. The experimental work of subsequent investigators has shown that v. Voit's results were due to a faulty analysis of the food consumed; that if certain errors are eliminated, all the carbon arising from protein metabolism can be detected in the usual excretions. The prevailing opinion is that fat does not arise from protein.

The appearance of fat granules in the cells of tissues undergoing certain pathologic changes was formerly regarded as evidence that the protein constituents of these cells in their metabolism give rise to fat. This view is also no longer entertained. The facts observed lead to the inference that the fat thus appearing is either transported from the connective-tissue cells or is deposited directly from the blood-stream; but owing to the destructive changes in the cell it is no longer able to metabolize it. The fat observed in muscle- and gland-cells is to be regarded as an evidence of deposition rather than of degeneration.

2. *From Fat.*—If now body fat is not a derivative of protein, the only two other sources are the fats and the carbohydrates of the food. That the fat of the food can be deposited is now a general belief, contrary to the former belief, that the fat of the food was at once oxidized, thus sparing from oxidation the fat arising from the protein. This belief is based on the results of experiments which however are not strictly physiologic in character. Thus two dogs were starved for a definite period. One was then given a large amount of linseed-oil and the other large amounts of mutton fat. At the end of several weeks both had accumulated fat. A post-mortem examination of the fat of the first dog showed that it was liquid at 0°C. while the fat of the second dog was solid at 50°C. In another experiment a dog

was allowed to starve until its weight had been reduced 40 per cent. It was then given large amounts of fat with small amounts of meat. At the end of five days, the animal was killed and found to contain 1353 grams of fat. Of this amount only 131 could have come from the protein. The inference therefore is that the food fat is capable of being deposited as such. The presence in the animal's fat of foreign fat acids such as erucic acid has been detected when the animal has been fed on colza or rape-seed oil.

Though these facts hold true it is highly probable that under physiologic conditions all the varieties of fats consumed as foods are digested and subsequently synthesized by the epithelial cells of the villi into the form of fat characteristic of the animal, and if not immediately needed for oxidation purposes is transported to the connective tissues and deposited. Regardless of the nature of the fat in the food, the fat of the animal is peculiar to it and possesses physical and chemic properties which serve in large measure to distinguish it.

3. *From Carbohydrates.*—That carbohydrates are capable of being transformed into fat when consumed in amounts beyond that necessary for heat-production is a generally well-recognized fact, though the successive steps by which this is brought about have never been disclosed. It has not been possible to effect this transformation by any known chemic procedure. Animals fed on a diet containing the customary amounts of protein and fat but containing a somewhat larger amount of carbohydrates than usual soon begin to lay on fat. The many experiments on the fattening of animals have placed this beyond question. This article of food must be looked on as the chief source of the body fat.

THE METABOLISM OF THE CARBOHYDRATES

It was stated in a previous chapter that all the starch and sugar that are consumed daily are converted by the action of the salivary, pancreatic and intestinal enzymes, for the most part into glucose; that after absorption the glucose is transported by the blood of the portal vein to the liver; that while passing through the liver capillaries, a portion passes across the capillary wall into the surrounding lymph and into the liver cells in which it is dehydrated by enzymic action and converted into starch (glycogen); that subsequently this starch is again hydrated by the same or a different enzyme and converted into sugar, glucose or glycose, after which it passes into the blood to take the place of the sugar which has left the blood and which has been oxidized in the tissues. By this process, glycogenolysis, the normal percentage of the sugar in the blood is maintained. The metabolism of the carbohydrates in the body includes a brief statement of the formation of glycogen and sugar in other tissues than the liver and more especially in the muscles.

Muscle Glycogen.—Glycogen is also found in muscles and to some extent in the placenta, and embryonic tissues generally. Chemic analysis has shown that muscles contain from 0.5 per cent. to 1 per cent. and as these organs amount to about 40 per cent. (28 kgm.) of weight of the body, 70 kgm., they generally contain from 140 to 280 grams of glycogen. Inasmuch as chemic analysis has failed to demonstrate the presence of glycogen in the blood, the inference is that it arises in the muscle-cell in a manner similar to that observed in the liver-cell, viz.: by a transformation, through de-hydration, of the sugar of the blood. By reason of this fact it may be said that the muscle also possesses a starch-forming or a *glycogenic* or an *amylogenetic* function. If it is a fact that of the sugar absorbed only from 12 to 20 per cent. is temporarily arrested by the liver, the remainder passing on into the blood of the general circulation, it is readily conceivable that the storage of the sugar under the form of glycogen by the muscle-cells is necessary not only for the activity of the muscle itself, but as a means of preventing an abnormal percentage of sugar in the circulating blood. It is generally admitted that though the glycogen is the source of the energy expended by the muscle, it cannot be disrupted and oxidized as such, but that it must first be transformed into sugar (glucose); and for this purpose the assumption is made that a special enzyme is present and active. The muscle is therefore said to possess or exhibit a sugar-forming or a *glycogenetic* function. The muscle-cells are thus like the liver cells characterized by the two processes amylogenesis and glycogenesis. During the periods of prolonged activity of the muscles the percentage of glycogen rapidly diminishes, a fact that leads to the inference that it is the source in large part of the energy expended by the muscle. During the period of rest the percentage of glycogen rapidly increases until the normal is regained.

The Influence of the Nerve System.—The physiologic mechanism by which glycogen is changed to glucose (glycogenolysis) in amounts just sufficient to supply the needs of the tissues without perceptibly increasing the amount of sugar in the blood is obscure and but imperfectly known. That the nerve system is in some way concerned in the regulation of glycogenolysis is apparent from observation of the effects of injuries, major emotional states as well as of the results of experimental procedures, but whether the regulation is *direct*, *i.e.*, through its action on the liver-cells, or *indirect*, *i.e.*, through its action on the glands of internal secretion, *e.g.*, adrenals and hypophysis, is a subject of investigation and discussion. It was discovered by Bernard that puncture of the floor of the fourth ventricle, at a point between the acoustic and vagus nerves, near the middle line, is followed within an hour or two by the appearance of sugar in the urine, which lasts for from five to six hours in the rabbit and from two to three or even seven in the dog. For this reason Bernard gave to this area the name of "diabetic area."

Coincident with the appearance of sugar in the urine (glycosuria) there is an increase in the percentage of sugar in the blood (hyperglycemia). The liver at the same time contains a higher percentage of sugar than normally. Apparently the initial step in this series of phenomena is an increased conversion of glycogen into sugar (glycogenolysis). This supposition receives support from the fact that the degree of the hyperglycemia, and the subsequent glycosuria, will depend on the amount of glycogen previously in the liver. If the animal has been well fed on carbohydrates, the resulting glycosuria will be pronounced; if, on the contrary, it has been allowed to fast for several days, the glycosuria will be slight.

Assuming that the nerve-cells, which constitute the diabetic area, influence the conversion of glycogen into sugar, the question arises as to whether the puncture destroys the nerve-cells, or whether it stimulates them in some way to increased activity. The results of experiment lead to the latter supposition. Thus stimulation of sensor nerves in different regions of the body, injuries to the central nerve system, major emotional states, etc., which have the same effect as puncture of the medulla lead to the inference that the "diabetic center" is stimulated by the puncture and hence to the further inference that normally it is stimulated by nerve impulses transmitted to it from one or more regions of the body. As to whether the puncture of the medulla excites the activities of vaso-motor or of secretor cells there is much obscurity. Whatever the nature of the impulses thus generated, the further question arises, as to the pathway by which the nerve impulses pass, whether by way of the vagi or by way of the spinal cord and the splanchnic nerves and the hepatic plexus formed in part by the post-ganglionic fibers from the cells of the semilunar ganglion. That it is not, by way of the vagi, is shown by the fact that division of these nerves does not interfere with the development of glycosuria, nor prevent it, after it is once established. That the pathway is down the spinal cord and subsequently through the splanchnics, is indicated by the fact that a transverse division of the spinal cord above the level of origin of these nerves, as well as a division of the splanchnics, prevents the development of the glycosuria that otherwise would follow puncture of the medulla. It must be remembered, however, that a transverse division of the spinal cord in itself frequently gives rise to a temporary glycosuria. Though the results of experimentation are not in all respects in agreement, yet there is evidence that the pathway is continued through the splanchnic nerve particularly on the left side as far as the semilunar ganglion and thence through the hepatic plexus.

Though stimulation of the left splanchnic nerve is usually followed by glycosuria, the question arises whether this effect is due to direct nerve stimulation of the liver cells, thus increasing glycogenesis or glycogenolysis, or whether it is due to an increased amount of adrenal secretion in the blood, which is discharged into it during the time of splanchnic stimulation. The following facts will serve to elucidate the relationship between these organs.

It is well known that the subcutaneous injection of one milligram of adrenalin chlorid per 1000 grams of body-weight, will give rise to hyperglycemia and glycosuria. Stimulation of the left splanchnic nerve just where it sends branches to the adrenal gland, gives rise to an increased secretion and its discharge into the blood as can be shown in many ways. From this the deduction is made that the glycosuria is the result of an increase in the normal percentage of adrenalin in the blood and this latter fact, is due to splanchnic stimulation. This supposition is strengthened by the further fact that after removal of the adrenal glands, neither puncture of the medulla nor stimulation of the splanchnics gives rise to glycosuria except in rare instances.

It is not to be inferred, however, that the mere presence of adrenalin in the blood is the cause of the increased activity of the liver cells and hence of the hyperglycemia and glycosuria. That another factor is present is evident from the following: Stimulation of the hepatic plexus, which presumably influences the production of sugar, always gives rise to glycosuria when the adrenal glands are intact but never after their removal. Hence the assumption is made that the production of sugar by the liver—glycogenolysis—is under the control of the central nerve system and by the route detailed in foregoing paragraphs, but only when a sufficient amount of adrenalin is present in the blood. The rôle assigned to the adrenalin is a heightening of the irritability of the terminal branches of the hepatic plexus whereby arriving nerve impulses become more efficient. These facts do not decide the question, however, as to the character of the nerves involved, that is, whether they are purely vaso-motor or secretory in character. The evidence for the existence of glycogenolytic nerves is not decisive.

Glycosuria.—The mechanism by which the sugar is stored in the liver as glycogen, and subsequently transformed into glucose, and discharged into the blood in amounts just sufficient to meet the needs of the tissues without giving rise to hyperglycemia and glycosuria, as well as the mechanism by which it is oxidized is apparently very delicate and easily disturbed as indicated by the ease with which a glycosuria more or less pronounced and of longer or shorter duration can be established. The causes of glycosuria are many and their mode of action often obscure.

Alimentary Glycosuria.—When carbohydrate food, sugar more especially is consumed in amounts beyond what constitutes the assimilation or storage limit, the excess soon appears in the urine. This limit varies somewhat in different animals. The tissues collectively of a normal human being have an assimilation capacity of approximately 150 grams of glucose. Should an amount of sugar be consumed much beyond this at one time, the excess will be eliminated in the urine. Inasmuch as carbohydrate material consumed each day is represented mainly by starch, and as digestion and absorption proceed slowly and metabolism continually, a glycosuria due to a large amount of aliment is not of frequent occurrence, under physiologic conditions. The assimilation limit may be lowered or raised beyond the normal in accordance with variations in the activity of the hypophysis. (See chapter on Internal Secretion.)

Adrenal Glycosuria.—As stated in a previous paragraph the subcutaneous injection of adrenalin chlorid or of the watery extract of the medulla of the gland is very soon followed by a glycosuria and hyperglycemia as well. The degree of the glycosuria will depend on the extent to which glycogen has been stored in the liver. It will also be recalled that stimulation of the left splanchnic nerve is followed by glycosuria by reason of a greater discharge of adrenalin into the blood. The increased transformation of glycogen to sugar has been attributed to an exaltation of the irritability of the nerve endings of the hepatic plexus or to a direct action on the liver cells themselves. As to which view is more probable, future experiments may decide. In either case the adrenalin excites an increased transformation of glycogen to sugar. Any factor therefore which would more or less permantly increase adrenal activity would cause a more or less permanent glycosuria. (See page 504.)

Pancreatic Glycosuria.—It has been known for some years that if the pancreas be extirpated and the animal survive the operation, glycosuria is promptly established, followed by a series of symptoms which gradually, increasing in severity, and lead to the death of the animal in from two to four weeks. In addition to the presence of sugar, acetone, aceto-acetic, β-oxybutyric acid, and an excess of urea have been found in the urine. The quantity of sugar excreted and the gravity of the attendant symptoms may be much diminished, if not entirely prevented by allowing a portion of the gland to remain even though its capacity for the production of pancreatic juice is entirely abolished. Transplantation of various portions of the pancreas into the subcutaneous tissue, in the walls of the abdomen, will also prevent the glycosuria. The explanations which have been offered as to the manner in which the pancreas prevents and its removal gives rise to the excretion of sugar are largely hypothetical.

It has been claimed by many investigators that the pancreas secretes a specific material partaking of the nature of a hormone which is discharged into the blood and by it distributed to various tissues, especially the muscles where it exerts its influence. Since the discovery of the islets of Langerhans in the body of the pancreas it has come to be believed that the cells composing these islets, rather than the cells lining the pancreatic acini generate the specific material. This view is supported by the fact that in many cases of persistent and fatal glycosuria in man, there is in the large majority of cases, a concomitant lesion of these islets. The route by which the secreted material reaches the blood is thought to be through the lymph-vessels and thoracic duct, for ligation of this latter vessel is followed glycosuria.

As to the manner in which the specific material prevents and its removal gives rise to glycosuria, two theories at least are supported by facts and are more or less plausible, *e.g.*:

1. That it promotes the oxidation (glycolysis) of sugar.
2. That it prevents a too rapid production of sugar on the part of the liver cells.

It is assumed according to the first view that there is present in the muscles, an enzyme, the action of which is the disruption of the sugar molecule and thereby promotes its oxidation; but that for the manifestation of its power it requires the activating influence of the pancreatic hormone, for in its absence oxidation of sugar does not take place and hence with the continual production of sugar by the liver cells, hyperglycemia and glycosuria result. This view has received confirmation in recent years from the results of the experimental work of Knowlton and Starling. These investigators were able, by employing a heart-lung preparation of a normal dog, to keep the heart beating for several hours in a practically normal manner by causing blood of the same animal to circulate through its cavities and the coronary system at the rate of about 300 c.c. every two minutes. To this blood glucose was added. At the end of the experiment it was found that the amount of sugar oxidized was, on the average, 4 milligrams per gram of heart-muscle per hour. On substituting the heart-lung preparation of a dog that had been rendered diabetic by the removal of the pancreas it was found that the power of consuming sugar was reduced to a minimum or altogether lost by reason presumably of the absence of the pancreatic hormone. They then demonstrated that the heart of the diabetic animal acquired a sugar-consuming or oxidizing power on feeding it with the blood of a normal animal, the consumption being in one animal 2.9, 5.8, 8.1 milligrams per gram of heart-muscle in three consecutive hours, and in another experiment there was an average consumption of 3.55 milligrams. In another series of experiments it was demonstrated that the diabetic heart very promptly developed a sugar-consuming power on the addition to the blood of a boiled extract of the pancreas the consumption rising from almost nothing to 4 milligrams in the second hour. The deduction from these experiments is that the oxidation of sugar is dependent on the presence of a specific hormone secreted by the pancreas. If this same fact could be established for skeletal muscle, the view that the pancreatic hormone promotes and its absence prevents the oxidation of sugar would be generally acceptable.

It is assumed by the supporters of the second view that the production of sugar in the liver cells is regulated by two opposing factors or hormones, that secreted by the adrenal glands and that secreted by the pancreas, the former exciting, the latter inhibiting the process. In the absence of the pancreatic hormone the adrenal hormone unduly excites the production of sugar. The following facts support this view: After extirpation of the adrenals or ligation of the adrenal veins, by which the secretion is prevented from entering the venous blood, the removal of the pancreas is not followed as usual by glycosuria. The simultaneous injection of an extract of pancreas and an injection of that amount of adrenalin ordinarily necessary to produce glycosuria prevents its development.

Pharmacologic Glycosuria.—It is well known that various pharmacologic agents when introduced into the body frequently give rise to glycosuria, though the manner in which they do so is not always clear. Thus, the administration of ether, curare, the uranium salts, phlorhizin, etc., is generally followed by the elimination of sugar in varying amounts. Of these agents the one generally used for experimental purposes is:

Phlorhizin.—Phlorhizin is a glucosid obtained from the root bark of the cherry, plum and apple tree. It can readily be separated into glucose and phloretin on the latter of which its action depends. If, therefore, either phlorhizin or phloretin be injected subcutaneously or administered by the mouth, sugar very promptly will appear in the urine in amounts varying, with the dosage, from 5 to 15 per cent. This glycosuria is, however, temporary, but may be made more or less continuous by repeated injections at least three or four times daily. Coincidently there is a diminution in the percentage of sugar in the blood (hypoglycemia), the opposite condition to that observed in the glycosurias heretofore mentioned. Inasmuch as this deficiency calls for a larger discharge of sugar from the liver this organ and others as well, soon become free from glycogen especially if the animal be deprived of carbohydrate food. Experimental investigations lead to the conclusion that the seat of action of the phlorhizin is in the kidney itself (whether in the glomerular or in the renal epithelium is uncertain), in consequence of which the sugar of the blood is permitted to pass along with other constituents into the tubules and hence into the urine. As to the change which the kidney structures undergo under the action of phlorhizin not much is known. It has been assumed that ordinarily the sugar is in combination with colloid material in the blood and by reason of this combination cannot pass across the wall of the glomerular blood-vessels. Any uncombined sugar, as is the case in hyperglycemia, will diffuse readily in the urine. Under the influence of phlorhizin the kidney structure is presumed to acquire the power of breaking up this combination setting the sugar free, whereupon it at once diffuses into the urine. When phlorhizin is administered to an animal living on a meat and fat diet alone, after all sugar has been discharged from the body, sugar still appears in the urine indicating that it must have some other origin than the glycogen of the liver or other tissues. The ratio of the dextrose to the nitrogen in the urine—2.8 to 1 (Minkowski) or 3.65 to 1 (Lusk), a ratio which corresponds to that found in the urine of diabetic patients living on a meat-fat diet, leads to the conclusion that the sugar arises from the metabolism of protein in a manner already alluded to.

Pituitary Glycosuria.—It was discovered by Cushing during his experimental and surgical procedures incidental to the removal of the pituitary in whole or in part, that glycosuria frequently develops which, however, gradually passes away. Subsequently it was shown that mechanical or electrical stimulation of the intact posterior lobe gave rise to a similar glycosuria provided of course there was a sufficiently large amount of glycogen in the liver. This effect has been attributed to an increased discharge of the internal secretion of the posterior lobe into the cerebro-spinal fluid and finally into the blood, which in some way lowers the assimilation limit of the animal and hence leads to an elimination of sugar (see chapter on Internal Secretion).

Parathyroid Glycosuria.—When the thyroids and at least three of the parathyroid bodies are removed in animals, there is a disturbance of carbohydrate metabolism, a diminished tolerance for sugar, as shown by the appearance of glycosuria. A similar condition is established when three parathyroids and but one thyroid are removed. It would thus appear that the parathyroids rather than the thyroids have an influence, though undefined in the regulation of carbohydrate metabolism.

The problem of the storage of sugar in the body, its release and subsequent oxidation in accordance with metabolic needs is of great interest by reason of the fact that it is intimately related with that grave condition of persistent glycosuria seen in man and to which has been given the term:

Diabetes.—This term has been applied to a syndrome characterized by persistent hyperglycemia and glycosuria accompanied by thirst, wasting of the tissues and imperfect oxidation of the fats. The sugar discharged into the urine varies in amounts but continues even in the absence of all carbohydrate food. The condition is usually permanent, enduring for months or years but eventually terminating in the death of the individual.

The cause of the disease in each instance is not always clear nor the manner in which the storage, release or oxidation of the sugar is disturbed.

A characteristic feature of the disease is the continuous elimination of sugar even in the absence of carbohydrate food. Under these circumstances there is evidence that the sugar is derived from the protein consumed or from the protein of the tissues or from both. It is well known that in the metabolism of protein it undergoes a cleavage into an NH_2 element and an organic acid radicle. It is further known that the NH_2 element is combined successively with hydrogen and carbon dioxid to form ammonium carbonate which is transformed in the liver into urea; that the organic acid radical is converted into sugar. It has also been determined that the dextrose yielded in the metabolism of protein bears to the nitrogen yield, the ratio of 3.65 to 1, indicating that for every 3.65 grams of sugar and every gram of nitrogen 6.25 grams of protein have been metabolized. In diabetes, in the absence of carbohydrate from the diet, this ratio of dextrose to nitrogen in the urine, expressed by the symbol D : N, has been found to exist from which the deduction is made that the origin of the sugar is to be sought for in the metabolism of the proteins.

The necessity for heat-production leads to a larger consumption of fat and this in turn impairs or overtaxes the capacity of the body tissues for fat oxidation and hence there arises imperfectly oxidized cleavage products such as β-oxybutyric acid, aceto-acetic acid and acetone which are finally eliminated in the urine thus establishing the condition of acidosis.

It is, therefore, apparent that the phenomena of diabetes in man closely resemble the phenomena that arise in animals when the pancreas is removed; hence there is a general belief that destructive disease of the pancreas is the most frequent cause of diabetes.

From the foregoing facts it is clear that a glycosuria more or less pronounced may be due to the following causes:

1. An imperfect abstraction of sugar from the portal blood and its storage as glycogen by the liver cells.

   The imperfect abstraction and storage of sugar may be due to an impairment in the functional activities of the liver cells or to the ingestion and absorption of excessive quantities of sugar from the intestine. In the latter instances the resulting glycosuria is said to be of alimentary origin.

2. A too rapid conversion of glycogen to sugar on the part of the liver cells (glycogenesis or glycogenolysis).

   The increased conversion of glycogen to glucose may be due to impairment of the nerve-centers regulating the normal process or to stimulation of the liver cells by one or more hormones discharged into the blood in unusual quantities by some organ of internal secretion, *e.g.*, adrenalin. See page 504.

3. An incomplete oxidation of sugar (glycolysis) in the cells of muscle and perhaps other tissues as well, in consequence of which it accumulates in the blood beyond the normal amount, thus establishing the condition of hyperglycemia.

   The imperfect oxidation of sugar in the muscle-tissue is probably the result of an absence of the necessary glycolytic enzymes. The more rapid metabolism of the protein constituents of the tissues whereby their glucose radicals are liberated in large amount may be necessitated by the inability to oxidize the sugar normally brought to them by the blood.

The final disposition of sugar in the body is an oxidation to carbon dioxid and water. The chief if not the only intermediate stage is lactic acid. It appears from chemical relations that the molecule of sugar is transformed into two molecules of lactic acid and these in turn into carbon dioxid and water. In its final oxidation the contained energy is liberated as heat.

CHAPTER XXI

THE CENTRAL AND PERIPHERAL ORGANS OF THE NERVE SYSTEM

The nerve system has been resolved by histologic investigation into single morphologic units termed neurons. Though they have a common origin they have assumed different forms, in different regions of the system in the course of their development. Nevertheless it is apparent from an examination of their structure that they have many features in common. The neurons in their totality constitute the neuron or nerve tissue. Arranged in both a serial and a collateral manner into a regular and connected whole, they form the neuron or nerve system. The neurons, moreover, are grouped into more or less complexly organized masses termed organs which in accordance with their location may be divided into (1) central organs and (2) peripheral organs.

The Central Organs.—The **central organs of the nerve system** are the encephalon and the spinal cord, lodged within the cavity of the cranium and the cavity of the spinal or vertebral column respectively. The general shape of these two portions of the nerve system corresponds with that of the cavities in which they are contained. The encephalon is broad and ovoid, the spinal cord is narrow and elongated.

The *encephalon* is subdivided by deep fissures into four distinct, though closely related portions: viz., (1) the cerebrum, the large ovoid mass, occupying the entire upper part of the cranial cavity; (2) the cerebellum, the wedge-shaped portion placed beneath the posterior part of the cerebrum and lodged within the cerebellar fossæ of the cranium; (3) the isthmus of the encephalon, the more or less pyramidal-shaped portion connecting the cerebrum and cerebellum with each other and both with (4) the medulla oblongata (Fig. 226).

The *spinal cord* is narrow and cylindric in shape. It occupies the spinal canal as far as the second or third lumbar vertebra.

The central organs of the nerve system are bilaterally symmetric, consisting of distinct halves united in the median line. The cerebrum is subdivided by a deep fissure, running antero-posteriorly, into two ovoid masses termed *cerebral hemispheres;* the cerebellum is also partially subdivided into hemispheres; the isthmus likewise presents in the median line a partial division into halves; the medulla oblongata and spinal cord are subdivided by an anterior or ventral and a posterior or dorsal fissure into halves, a right and a left.

The Peripheral Organs.—The **peripheral organs of the nerve system** in anatomic and physiologic relation with the central organs are the encephalic and the spinal nerves.

The *encephalic nerves,* twelve in number on each side of the median line, are in anatomic relation with the base of the encephalon, and because of the fact that they pass through foramina in the walls of the cranium they are usually termed cranial nerves.

The *spinal nerves*, thirty-one in number on each side, are in anatomic relation with the spinal cord, and because of the fact that they pass through foramina in the walls of the spinal column they are termed spinal nerves. As both cranial and spinal nerves are ultimately distributed to the structures of the body—*i.e.*, the general periphery—they collectively constitute the *peripheral organs of the nerve system.*

The spinal nerves consist of two groups of nerve-fibers, a ventral and a dorsal group. Though closely intermingled in the common trunk of the spinal nerve they are distinctly separated near the spinal cord. Owing to their connection with the ventral and dorsal surfaces of the spinal cord they have been termed respectively the ventral and dorsal roots. Peripherally the ventral root fibers are distributed to skeletal muscles, glands, walls of blood-vessels and walls of various viscera: the dorsal root fibers are distributed to skin, mucous membranes, muscles, joints, etc.

The central organs of the nerve system are supported and protected by three membranes named, in their order from without inward, the dura mater, the arachnoid, and the pia mater.

The Encephalo-spinal Fluid.—The general subarachnoid space, as well as certain cavities within the encephalon, contain a clear transparent fluid, termed the encephalo-spinal fluid. This fluid has an alkaline reaction and a specific gravity of 1.007 or 1.008. It is composed of water, proteins (proteoses and serum globulin), and pyrocatechin $C_6H_4(OH)_2$, capable of reducing copper salts, though not exhibiting any other of the properties of sugar. In many respects this fluid resembles lymph. The subarachnoid space and the general encephalic cavities, termed ventricles, communicate with one another by an opening in the pia mater (the foramen of Magendie) as it passes over the lower part of the fourth ventricle.

The Functions of the Nerve System.—It will be recalled that the entire nerve system can be resolved into simple morphologic units, termed neurones, each of which possesses certain histologic features and physiologic properties; that their relation one to the other both in a serial and collateral manner gives rise to the general architecture of the nerve system. Recalling the functions of neurons in their individual and collective capacities the functions of the nerve system may be formulated.

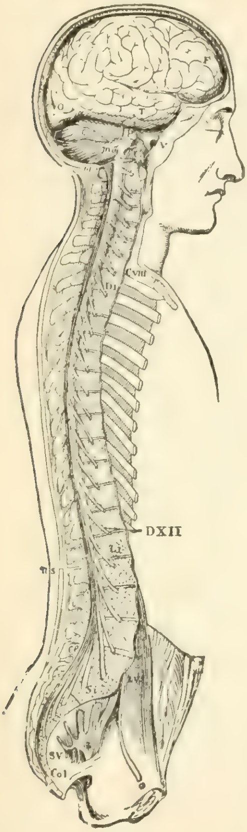

FIG. 226.—THE CENTRAL ORGANS OF THE NERVE SYSTEM. F. T. O. Frontal, temporal, and occipital lobes of the cerebrum. C. Cerebellum. P. Pons. *mo.* Medulla oblongata. *ms.*, *ms.* The upper and lower limits of the spinal cord. The remaining letters indicate the region and number of the spinal nerves.—(*Quain, after Bourgery.*)

The functions of the nerve system are twofold: (1) It unites and associates the organs and tissues of the body in such a manner that they are enabled to coöperate for the accomplishment of a definite object. (2) It serves to arouse in the individual a consciousness of the existence of an external world, by virtue of the impressions which it makes on his sense organs, and consequently to enable him to adjust himself to his environment.

By virtue of the anatomic and physiologic association, a stimulus, if of sufficient intensity, applied to one organ or tissue will call forth activity in one or more organs near or remote from the part stimulated. This coördination of action is accomplished mainly by the spinal cord and the medulla oblongata. All actions which take place in response to a peripheral stimulus and independently of volition are termed reflex actions. The reflex activities connected with digestion, the circulation of the blood, with respiration, excretion, etc., are illustrations of the coördinating capabilities of the nerve-centers located in these portions of the central nerve system.

By virtue of the physiologic activities of the encephalon and more particularly of the cerebrum and of the relation existing between it and the sense organs of the body, consciousness of the existence of an external world and the individual's relation to it is developed. Experimental and clinic investigations show that of the parts of the encephalon, the cerebrum is the chief, though not perhaps the sole organ of the mind and that its functions are for the most part mental.

The function of a part at least of the peripheral nerve system is to afford a means of communication between the central organs of the nerve system and the remaining structures of the body.

The nerve-trunks constituting this part of the nerve system may be divided into two groups, as follows:

1. The first group comprises nerves in connection with the special sense-organs, *e.g.*, skin, eye, ear, nose, tongue, as well as nerves in connection with the general or organic sense-organs, *e.g.*, mucous membranes, viscera, etc., which are connected primarily with nerve-cells in the spinal cord and medulla oblongata, and secondarily with nerve-cells in localized areas of the cerebral cortex.
2. The second group comprises nerves which terminate mainly in the muscle apparatus and which constitute the continuation of nerve paths which have their origin in nerve-cells of localized areas of the cerebral cortex.

The first group of nerves, the *afferent*, especially those connected with the special sense-organs, are excited to activity by impressions made on their peripheral terminations by agencies in the external world. The nerve impulses thus generated are transmitted in part only as far as the spinal cord and medulla oblongata while the remainder ascend to nerve-cells in localized areas of the cerebral cortex where they evoke sensations. These sensations by their grouping and combinations become the primary elements of intelligence. The afferent nerves thus become a means of communication between the physical and the mental worlds.

The second group of nerves, the *efferent*, are excited to activity by those molecular disturbances in their related nerve-cells which accompany volitional efforts. The nerve impulses thus developed and discharged from localized areas in the cerebral cortex are transmitted by way of the medulla and spinal cord to the muscles of the face, trunk and extremities which are in consequence excited to activity. The muscle movements thus become physical expressions of mental states, and if directed in a definite manner to the overcoming of the resistance offered by the external world they become capable of modifying it in accordance with the mental states. The efferent nerves thus become a means of communication between the mental and the physical worlds.

The central nerve system is thus composed of a number of separate though closely related parts, to each of which a separate function has been assigned. In the study of the structure and function of these separate parts it will be found convenient, and conducive to clearness, after a brief presentation of the relation of the spinal nerves to the spinal cord, to consider them in the order of their complexity, beginning with the spinal cord and ending with the cerebrum.

The Relation of the Spinal Nerves to the Spinal Cord.—The spinal nerves present near the spinal cord two divisions which from their connection with the anterior or ventral and the posterior or dorsal surfaces are known as the ventral and dorsal roots.

The *ventral* roots are the axons of various groups of nerve-cells situated in the anterior horns of the gray matter. From their origin these axons pass almost horizontally forward through the anterior column in three distinct bundles. After emerging from the cord they curve downward and backward to join the dorsal roots.

The *dorsal* roots are the centrally directed axons of nerve-cells in the spinal ganglia. After entering the cord they divide into two main groups, a lateral and a mesial. A portion of the lateral group enters the posterior horn directly through the caput cornu; the other portion turns upward and runs through Lissauer's tract and ultimately enters the posterior horn. The mesial group passes into the postero-external column (Burdach), where the fibers divide into descending and ascending branches. The former probably constitute the comma tract, the terminal branches of which surround cells in the gray matter; the latter (ascending) cross the column obliquely and enter the postero-internal column (Goll), in which they pass upward to terminate around the cells of the nucleus gracilis of the same side. As these root fibers pass up and down the cord, collateral branches are given off which enter the gray matter at successive levels and come into physiologic relation with the cells of Clark's vesicular column on the same and opposite sides and with the cells of the anterior horn.

The peripherally directed axons of the nerve-cells in the spinal nerve ganglia become associated with the axons of the ventral roots and together they pass as a spinal nerve to peripheral organs.

Classification of Spinal-nerve Fibers.—The ventral root axons have been shown by histologic and physiologic methods of investigation to be distributed to skeletal muscles, glands, blood-vessels, and viscera. The dorsal root axons have been shown by the same methods to be distributed to skin, mucous membranes, and muscles. Hence the ventral and dorsal root fibers may be classified in accordance with their distribution, and the characteristic modes of activity to which they give rise into several groups as shown in the tabulation on pages 99, 100.

Though both the efferent and afferent fibers of the spinal nerves are directly connected with nerve-cells in the spinal cord, they are also indirectly connected by efferent and afferent nerve-tracts with the cerebral cortex.

Experimentally, it has been determined that the anterior or ventral roots contain all the *efferent* fibers, the posterior or dorsal roots all the *afferent* fibers. The proofs in support of this view are as follows:

Stimulation of the ventral root fibers produces:

1. Tetanic contraction of skeletal muscles.
2. Discharge of secretions from glands.
3. Increase in the degree of the contraction, the tonus, of the muscle walls of the peripheral arteries.
4. Variations in the degree of the contraction, the tonus, of the muscle walls of certain viscera either in the way of augmentation or inhibition.[1]

Division of the ventral root fibers is followed by:

1. Relaxation of skeletal muscles and loss of movement.
2. Cessation in the discharge of secretions from glands.
3. Temporary dilatation and loss of the tonus of blood-vessels.
4. Temporary impairment of the normal activities of the visceral muscles from loss of central nerve control; the degree of impairment depending on the nature of the viscus involved.

Peripheral stimulation of the dorsal root fibers produces:

1. Reflex excitation of spinal centers, in consequence of which there is an increased activity of skeletal muscles, glands, blood-vessels, and visceral walls.
2. Reflex inhibition of spinal nerve-centers, in consequence of which there may be a decrease in the activities of skeletal muscles, glands, blood-vessels, and viscera.
3. Sensations of touch, temperature, pressure, and pain.
4. Sensations of the duration and direction of muscle movements, of the resistance offered and of the position of the body or of its individual parts (muscle sensations).

Division of the dorsal root fibers is followed by:

1. Loss of the power of exciting or inhibiting reflexly the activities of spinal nerve-centers and in consequence a loss of the power of exciting or inhibiting the activities of peripheral organs.
2. Loss of sensation in all parts to which they are distributed.

The ventral roots are therefore efferent in function, transmitting nerve impulses from the spinal cord to the peripheral organs which excite them to activity.

The dorsal roots are afferent in function, transmitting nerve impulses from the general periphery to (*a*) the spinal cord where they excite its contained nerve-centers to activity or to a more or less complete cessation of activity (inhibition), and (*b*) to the cerebrum where they excite its centers to activity with the development of sensations.

The Relation of the Encephalic Nerves to the Encephalon.—The encephalic or cranial nerves consist of efferent and afferent fibers. The two groups of fibers, however, are not comprised in a single nerve trunk as are the corresponding fibers of the spinal nerves but pass for the most part to their destinations as independent and distinct nerves. These nerves also serve as a means of communication between the encephalon and the peripheral organs.

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[1] These last three phenomena are especially associated with the ventral roots of the second thoracic to the third or fourth lumbar nerves inclusive.

The efferent nerves taken collectively are also distributed to skeletal muscles, glands, blood-vessels and viscera.

The afferent nerves taken collectively are distributed to the skin, mucous membrane and to specialized sense organs—eye, ear, nose, tongue and skin. Some of the afferent nerves contain efferent fibers which are distributed to glands, blood-vessels and viscera.

The origin and distribution of both efferent and afferent encephalic nerves and the phenomena that follow their stimulation and divisions, and the functions attributed to them will be fully considered in a subsequent chapter.

THE SPINAL CORD

The narrow elongated portion of the central nerve system contained within the spinal canal is named, from its situation and appearance, the spinal cord. It is cylindric in shape though presenting an enlargement in both the lower cervical and lower lumbar regions corresponding to the origins of the nerves distributed to the upper and lower extremities. The cord varies in length from 40 to 45 cm., measures 12 mm. in diameter, weighs 42 gms., and extends from the atlas to the second lumbar vertebra, beyond which it is continued as a narrow thread, the *filum terminale.* It is divided by the anterior and posterior longitudinal fissures into halves, and is therefore bilaterally symmetric. A transverse section of the cord shows that it is composed of both white and gray matter, the former covering the surface, the latter occupying the center.

The Segmentation of the Spinal Cord.—For the elucidation of many problems connected with the physiologic actions of the spinal cord, as well as of the symptoms which follow its pathologic impairment, it will be found helpful to consider the cord as consisting physiologically of a series of segments placed one above the other, the number of segments corresponding to the number of spinal nerves. Each spinal segment would therefore comprise that portion of the cord to which is attached a pair of spinal nerves. The nerve-cells in each segment are in histologic and physiologic relation with definite areas of the body, embracing muscles, glands, blood-vessels, skin, etc.

If the exact distribution of the nerves of any segment were known, its function could be readily stated. By virtue of this segmentation it becomes possible for each segment to act independently of or in coöperation with other segments near or remote, with which they are associated by the intrinsic or associative cells and their axons; and by the same coöperative action the spinal cord itself is enabled to act as a unit.

The Structure of the Gray Matter.—The gray matter is arranged in the form of two crescents, united in the median line by a transverse band or commissure forming a figure resembling the letter **H.** Though varying in shape in different regions of the cord, the gray matter in all situations presents on either side an anterior or ventral and a posterior or dorsal horn. Between the two horns there is a portion termed the intermediate gray substance. The commissure presents in its center a narrow canal which extends throughout the entire length of the cord. This canal is lined by cylindric epithelium and surrounded by gelatinous material. (Fig. 227.)

The *anterior horn* is short and broad and entirely surrounded by white matter. The *posterior horn* is narrow and elongated and extends quite up to the surface of the cord, where it is capped by gelatinous matter, the *substantia gelatinosa.* In the lower cervical and thoracic regions a portion of the intermediate gray substance projects outward and forms the so-called lateral horn. The gray matter fundamentally consists of a framework of fine neuroglia supporting blood-vessels, lymphatics, medullated and non-medullated nerves, and groups of nerve-cells.

The Nerve-cells.—The nerve-cells of the cord are very numerous and they present a variety of shapes and sizes in different regions. They are usually arranged in groups which extend for some distance up and down the gray matter, forming columns more or less continuous.

In the anterior horn two well-marked groups are found, one situated at the anterior and inner angle, known as the antero-median group, the other situated at the posterior and lateral angle and known as the postero-lateral group. In the lower cervical and upper thoracic regions, in the region of the lateral horn, another group of cells is found, known as the intermediate group. In the central portion of the horn there is also a central group.

The cells of the anterior horns are of large size, nucleated and multipolar. They are the modified descendants of pear-shaped cells, the neuroblasts, which migrated from the medullary tube (see page 97). In the course of their migration they developed dendrites which form an intricate felt-work throughout the anterior horn. One of the processes, the axon, approached the surface of the cord, penetrated it, grew outward, became covered with myelin and neurilemma, and developed into an anterior root fiber. These nerve-cells, with their dendrites, axons, and terminal branches, form efferent neurons of the first order. The intimate histologic and physiologic relationship existing between the nerve-cell and the axon is revealed by the degenerative changes which arise in the latter when separated from the former. The cell apparently determines the nutrition of the axon and may be regarded as trophic in function. Some of the cells of the anterior horn send their axons into the immediately surrounding white matter of the same side, after which they divide into two branches, one passing up, the other down, the cord, to reënter the gray matter at different levels. They are probably associative in function. Other cells send their axons into that portion of the white matter on the same and opposite sides known as Gower's antero-lateral tract (Fig. 228).

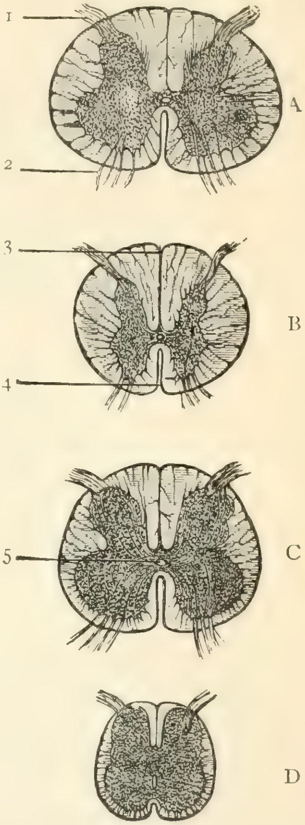

FIG. 227.—SECTIONS THROUGH DIFFERENT REGIONS OF THE SPINAL CORD. A. At the level of the sixth cervical nerve. B. At the mid-dorsal region. C. At the center of the lumbar enlargement. D. At the upper part of the conus medullaris. 1. Posterior roots. 2. Anterior roots. 3. Posterior fissure. 4. Anterior fissure. 5. Central canal.—(*Morris' "Anatomy," after Schwalbe.*)

In the posterior horn nerve-cells are also present, though they are not so numerous as in the anterior horn. At the base of the horn and on its inner side there is a well-marked group of cells which extends from the seventh or eighth cervical nerves downward to the second or third lumbar nerves, being most prominent in the thoracic region. This column is known as Clarke's vesicular column. From the nerve-cells constituting this column axons pass obliquely outward into the portion of the white matter known as the direct cerebellar tract. Other nerve-cells send their axons into the white matter in the posterior portion of the cord bordering the posterior median fissure. Some of the nerve-cells, their situation and the distribution of their axons are shown in Fig. 228.

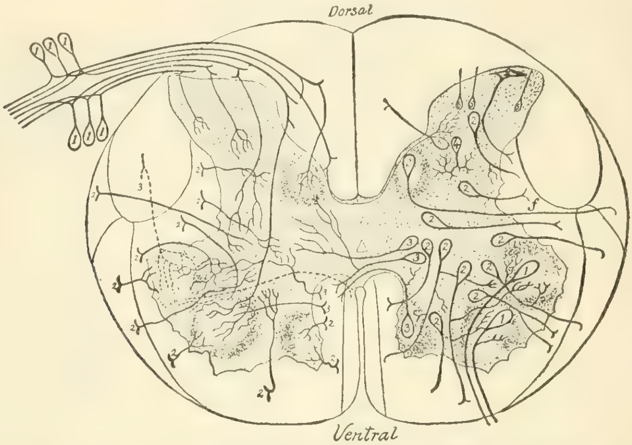

FIG. 228.—SCHEME OF THE STRUCTURE OF THE CORD.—(*Howell after Lenhossek.*) On the right the nerve-cells; on the left the entering nerve-fibers. Right side: 1, Motor cells, anterior horn, giving rise to the fibers of the anterior root; 2, tract cells whose axons pass into the white matter of the anterior and lateral columns; 3, commissural cells whose axons pass chiefly through the anterior commissure to reach the anterior columns of the other side; 4, Golgi cells (second type), whose axons do not leave the gray matter; 5, tract cells whose axons pass into the white matter of the posterior column. Left side: 1, Entering fibers of the posterior root, ending, from within outward, as follows: Clarke's column, posterior horn of opposite side, anterior horn same side (reflex arc), lateral horn of same side, posterior horn of same side; 2, collaterals from fibers in the anterior and lateral columns; 3, collaterals of descending pyramidal fibers ending around motor cells in anterior horn.

Classification of Nerve-cells.—The cells of the gray matter may be divided into three main groups: viz., intrinsic or associative, receptive or afferent, and emissive or efferent.

The *intrinsic cells* are associative in function. The axons to which these cells give origin pass more or less horizontally into the white matter, where they divide into two branches, one of which passes upward, the other downward. At various levels they reënter the gray matter and arborize around other intrinsic cells.

The *receptive cells* are largely sentient or afferent in function, inasmuch as the excitations brought to the spinal cord by the afferent nerves in the dorsal roots from the general periphery are received by them and transmitted by and through their axons to the cortex of the cerebrum, where they are translated into conscious sensations. As the nerve-fibers in the dorsal roots of the spinal nerves are classified, in accordance with the sensations to which they give rise, as sensor, thermal, tactile, etc., so these nerve-cells may be similarly classified according as they transmit their excitations to those specialized areas in the cerebral cortex in which these different sensations arise.

The *emissive cells* are efferent or motor in function, inasmuch as the excitation arising in them is transmitted outwardly through their axons to muscles, glands, blood-vessels and viscera, imparting to them motion, either molar or molecular. As the efferent fibers in the ventral roots of the spinal nerves are classified (see page 99) in accordance with their physiologic action into motor, secretor, vaso-motor, viscero-motor and pilo-motor nerves, so the nerve-cells of which the nerves are integral parts may be classified physiologically as motor, vaso-motor, secretor, viscero-motor and pilo-motor. Collections or groups of such cells are termed "centers."

The Structure of the White Matter.—A transverse section of the cord shows that the white matter completely covers the gray matter except where the posterior horns reach the surface. Anteriorly the white matter of each lateral half is connected by a narrow strip or bridge of white matter, the anterior commissure. Microscopic examination shows that the white matter is composed of vertically disposed medullated nerve-fibers which are devoid of a neurilemma. These fibers are supported partly by a framework of connective tissue, and partly by neuroglia. The white matter of each side of the cord is anatomically divided into an anterior, a lateral, and a posterior column by the anterior and posterior roots of the spinal nerves.

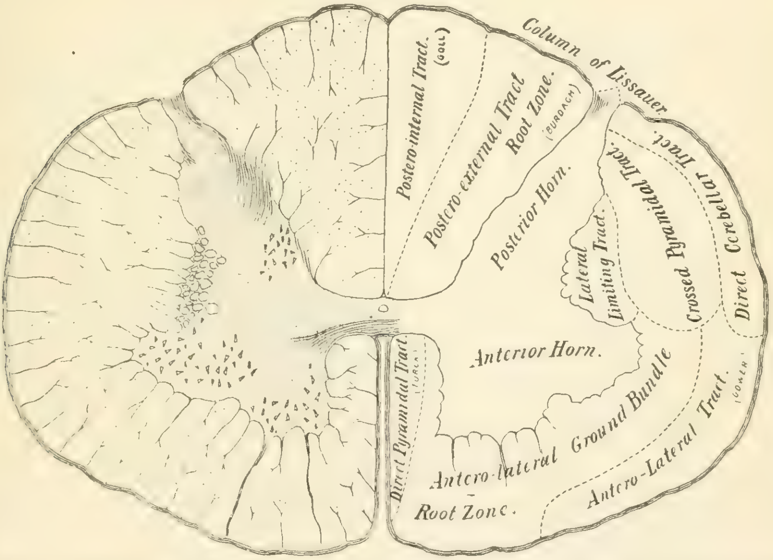
Column of Lissauer.
Postero-internal Tract.
(GOLL)
Postero-external Tract
Root Zone.
(BURDACH)
Posterior Horn.
Lateral Limiting Tract.
Crossed Pyramidal Tract.
Direct Cerebellar Tract.
Anterior Horn.
Direct Pyramidal Tract.
(TURCK)
Antero-lateral Ground Bundle
Antero-Lateral Tract.
(GOWER)
Antero-lateral Root Zone.

FIG. 229.—TRANSECTION OF THE CERVICAL SPINAL CORD SHOWING ITS CHIEF SUBDIVISIONS.—(*After Mills.*)

Classification of the Nerve-fibers.—From a study of the embryologic development of the white matter and of the degenerative changes which follow its pathologic and experimental destruction, it has been differentiated into a number of specialized tracts which have different origins, destinations, and functions. Some of the more important tracts are shown in Fig. 229. They may be divided, however, into efferent, afferent, and associative fibers.

1. The **anterior column**, comprising that portion between the anterior longitudinal fissure and the anterior roots, has been subdivided into:

(*a*) The *direct pyramidal tract*, or column of Türck. This tract borders the longitudinal fissure and extends from the upper extremity of the cord as far down as the mid-thoracic region. From above downward this tract diminishes in size, for the reason that its fibers or their collaterals cross at successive levels to the opposite side of the cord by way of the anterior commissure to enter the gray matter of the anterior horn. These fibers are the continuations of fibers which take their origin in cells which are located in the cortex of the cerebral hemisphere of the same side. The terminal filaments of these fibers or axons are in physiologic relation either directly or indirectly through intercalated neuron cells with the dendrites of the cornual cells. When divided in any part of their course, these fibers undergo descending degeneration.

(*b*) The *antero-lateral ground bundle or root zone.* This tract lies external to the pyramidal tract, surrounds the anterior horn of the gray matter, and extends throughout the length of the cord. It is composed of short commissural or associative fibers which come from nerve-cells in the gray matter from the same and opposite sides of the cord. After entering the white matter they divide into two branches, pursue opposite directions, then reënter the gray matter at higher and lower levels and come into relation with other nerve-cells:

2. The **lateral column**, comprising that portion between the ventral and dorsal roots, has been divided into:

(*a*) The *antero-lateral tract* of Gowers. This tract is somewhat crescentic in shape and situated on the lateral aspect of the cord external to the antero-lateral root zone. It extends throughout the entire length of the cord. When divided it undergoes ascending degeneration, which would indicate that the axons originate in nerve-cells in the gray matter. This tract is therefore probably afferent in function.

The majority of the fibers composing this tract on reaching the pons turn backward, pass through the superior medullary velum to terminate in the dorsal vermis of the cerebellum.

(*b*) The *lateral limiting tract.* This tract, which is quite narrow, lies close to the external border of the gray matter. It is composed of fibers which do not degenerate to any considerable extent after transverse section and are in all probability associative fibers which come from nerve-cells in the gray matter to reënter at lower and higher levels. It is also believed by some investigators that the anterior portion contains efferent and the posterior portion afferent fibers; for this reason it is frequently termed the mixed lateral tract.

(*c*) The *crossed pyramidal tract.* This tract occupies the posterior portion of the lateral column, though its exact position varies somewhat in different regions of the cord. In the cervical and thoracic regions it is covered by a layer of fibers. In the lumbar region, however, it comes to the surface. From above downward this tract gradually diminishes in size, for the reason that its fibers and their collaterals enter the gray matter at successive levels. The terminal branches of these fibers are in close physiologic relation either directly or indirectly through intercalated neuron cells with the dendrites of the cornual cells. These fibers are the continuations of fibers which take their origin in cells which are located in the cortex of the cerebral hemispheres of the opposite side. When divided in any part of their course, they undergo descending degeneration. They are therefore efferent neurons and of the second order.

(*d*) The *direct cerebellar tract*, or column of Flechsig. This tract is situated on the surface of the lateral column external to the crossed pyramidal tract. It slightly increases in size from below upward. It is composed of fibers the cells of which are found on the inner side and base of the posterior horn (Clark's vesicular column). From this origin the fibers pass obliquely outward to the surface and then directly upward to terminate, as its name implies, in the cerebellum. Decussation of these fibers takes place in the superior vermiform lobe of the cerebellum. When divided this tract degenerates upward. It is therefore in all probability an afferent tract and of the second order.

3. The **posterior column,** comprising that portion between the dorsal roots and the posterior longitudinal fissure, has been subdivided into:

(*a*) The *postero-external tract* of Burdach. This tract lies just within the posterior horns. A portion of this tract is composed of ground fibers which, though vertically disposed, have but a short course. They take their origin in cells in the gray matter, and after entering this tract divide into ascending and descending branches, which with their collaterals reënter the gray matter at different levels. Another portion of this tract is made up of nerve-fibers derived from the dorsal roots of the spinal nerves, which cross this column toward the median line in an oblique or horizontal direction. The fibers of the upper portion of this tract terminate around the *nucleus cuneatus* at the medulla oblongata. When divided, these fibers degenerate for but a short distance. The ground fibers are probably associative in function.

(*b*) The *postero-internal tract*, or column of Goll. This tract is separated from the former by a septum of connective tissue which is most marked above the eleventh thoracic segment. The fibers which compose this tract are long and derived for the most part from the dorsal roots of the spinal nerves of *the same side*. This is shown by the fact that division of these roots central to the ganglion is followed by ascending degeneration of the column of Goll as far as the *nucleus gracilis* in the medulla oblongata. Fibers derived from cells in the gray matter are also contained in this column. This tract is largely afferent in function.

(*c*) *Lissauer's tract*. This tract embraces the tip of the posterior horn and is composed principally of fibers from the dorsal roots of the spinal nerves. After entering the tract the fibers divide into ascending and descending branches, which finally terminate around cells in the posterior horn.

In addition to the tracts described in foregoing paragraphs a number of small narrow tracts have been discovered in different regions of the spinal cord the functional significance of which, however, has not been determined. Of these may be mentioned:

1. The *antero-lateral tract* of Marchi and Löwenthal, situated at the anterior and inner angle of the anterior column, which degenerates downward after removal of one-half of the cerebellum.

2. The *comma tract*, a narrow bundle of fibers situated in the anterior portion of the column of Burdach. When it is divided it degenerates downward.

3. The *septo-marginal tract*, an oval-shaped tract situated along the margin of the posterior longitudinal fissure.

4. The *cornu-commissural tract* found along the border of the anterior portion of the posterior column as far forward as the posterior commissure. Both of these tracts are best developed in the lumbosacral region. They arise from nerve-cells in the gray matter. They undergo descending degeneration when divided, but not after division of the dorsal roots.

THE FUNCTIONS OF THE SPINAL CORD

Anatomic investigation has demonstrated that the segments of the spinal cord are associated through their related spinal nerves with the organs and tissues of definite areas of the body. Physiologic investigation has also demonstrated that the segments by reason of the presence of nerve-cells and nerve-fibers may be regarded as composed of:

1. Nerve-centers, each of which has certain special functions, and
2. Conduction paths by which these centers are brought into relation not only with one another, but with the cerebrum and its subordinate or underlying parts, *e.g.*, the medulla oblongata, pons varolii and cerebellum.

A. THE SPINAL CORD SEGMENTS AS LOCAL NERVE-CENTERS.

The efferent cells of the spinal segments are the immediate sources of the nerve energy that excites activity in skeletal muscles, glands, vascular, and to some extent visceral muscles.

The discharge of their energy may be caused:

1. By variations in the composition of the blood or lymph by which they are surrounded or as the outcome of a reaction between the chemic constituents of the lymph on the one hand and the chemic constituents of the nerve-cell on the other hand. The excitation of the cell thus occasioned is termed *automatic* or *autochthonic* excitation.
2. By the arrival of nerve impulses, coming through afferent nerves from the general periphery, skin, mucous membrane, etc.
3. By the arrival of nerve impulses descending the spinal cord from cells in the cortex of the cerebrum or subordinate regions.

The excitation in the former instance is said to be *reflex* or *peripheral* in origin; in the latter instance *direct* or *cerebral* in origin. In the direct or cerebral excitations the skeletal muscle movements are due to psychic states of a volitional, or an affective or emotional character; the gland discharges and vascular and visceral muscle movements to affective or emotional phases of cerebral activity only.

Automatic Excitation.—By this expression is meant a discharge of energy from the spinal nerve-cells occasioned by (a) a change in the chemic composition of the blood or lymph by which they are surrounded or probably a reaction between the constituents of the lymph and the constituents of the nerve-cell or (b) the development within the cell of a stimulus, the so-called "inner stimulus," the outcome of metabolic activity.

As no effect arises without a sufficient cause the term automatic has been objected to and the term autochthonic has been suggested, as more nearly expressing the facts stated. A center so acting could not be regarded as primarily a center for reflex activity, however much it might be influenced secondarily by afferent nerve impulses. If the cell excitation is continuous though variable from time to time, it is said to possess tonus and the organ or tissue thus excited is also said to possess tonus or to be in a state of tonic activity. If the cell discharge is intermittent in character it imparts to certain muscles, *e.g.*, the respiratory muscles, a rhythmic activity. It must, however, be kept in mind that the tonus of nerve-centers as well as of peripheral organs can also be developed and maintained by the inflow of nerve impulses transmitted from the periphery. The reason for the belief that the cord and its upper prolongation, the medulla oblongata, are endowed with autochthonic activity is based on the fact that certain peripheral organs are in a state of continuous activity and apparently uninfluenced to any marked extent except temporarily by nerve impulses transmitted to the cord through afferent nerves. As illustrations of such continuous activity may be mentioned: (a) the contraction of the abductor muscle of the larynx (the posterior crico-arytenoid) whereby the vocal membranes are separated and the glottis kept open under all circumstances except during the emission of a vocal sound; (b) the contraction of the dilatator muscle of the iris; (c) the contraction of the anal and vesic sphincters; (d) the periodic contraction of the respiratory muscles (see page 425); (e) the acceleration of the heart-beat (page 423).

Though automatic activity of the spinal cord is yet upheld by some physiologists, the fact must be recognized that with increasing knowledge of reflex activities many phenomena previously regarded as automatic have been found to be dependent on peripheral stimulation and therefore reflex in origin. Whether this will eventually be found true for all instances of so-called automatic or autochthonic activity will depend on the results of future investigations. Among the phenomena removed from the sphere of automatic, to the sphere of reflex activity may be mentioned muscle tonus, vascular tonus and, trophic tonus.

Muscle Tonus.—All the skeletal muscles of the body are at all times in a state of slight but continuous contraction, termed tonus, by virtue of which their efficiency as quickly responsive organs is increased. That such a slight contraction is present even in a state of rest is shown by the fact that if a muscle be divided in the living animal the two portions will contract and separate to a certain distance. The condition of the muscle was formerly attributed to an automatic and continuous discharge of energy from the nerve-cells. Brondgeest, however, showed that this tonus is entirely reflex in origin and immediately disappears on division of the posterior roots of the spinal nerves, which would not be the case if the cells in the cord were acting automatically. The afferent nerves in this reflex arise in the muscle or its tendons, and the stimulus is the slight degree of extension to which the muscle is subjected in virtue of its attachments and the ever-varying position of the limbs and trunk (see page 57).

Vascular Tonus.—The arteriole muscles throughout the vascular apparatus are also constantly in a state of slight but continuous contraction which assists in the maintenance of an average arterial pressure and is due to the continuous discharge of nerve energy from the general or dominating vaso-tonic (constrictor) center in the medulla oblongata. This center it will be recalled has been shown by Porter to consist of two portions, a vaso-tonic and a vaso-reflex. The former is in a state of continuous tonus or activity; the latter is capable of being influenced in its activity not only by variations in the composition of the blood but by nerve impulses transmitted to it from all regions of the body (see page 383).

Trophic Tonus.—The normal metabolism of muscle, gland, and connective tissue which underlies the assimilation of food, the production and storage of energy-holding compounds, and the production of new compounds, is dependent, in the higher animals at least, on the connection of these tissues with the central nerve system; for if the efferent nerves be divided, not only will they themselves undergo degeneration in their peripheral portions, but the muscles, glands, and connective tissues to which they are distributed will also undergo similar changes. This is to be attributed not merely to inactivity, but rather to a loss of nerve influence. It would appear from facts of this character that the normal metabolism is dependent for its continuance on nerve influences. There is no evidence, however, as to the existence of special trophic nerves, separate from those which impart to glands and muscles their customary activities. The trophic centers and the motor centers are identical, though the two modes of their activity are separate and distinct. The activity of the so-called trophic centers which was at one time believed to be automatic is now regarded as due to reflex influences.

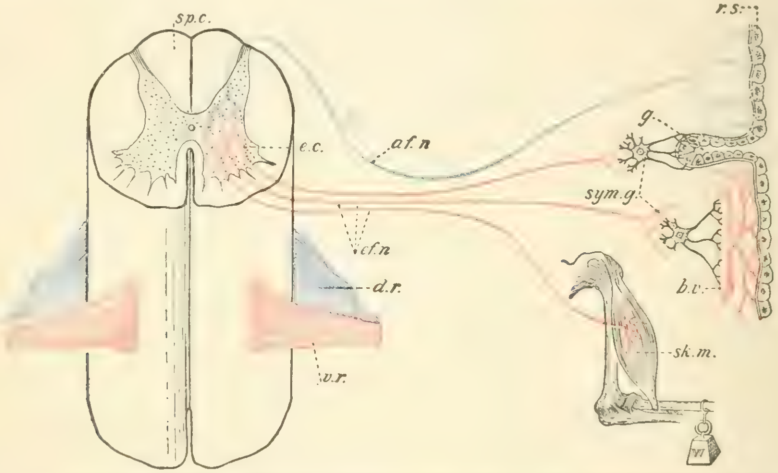

FIG. 230.—DIAGRAM SHOWING THE STRUCTURES INVOLVED IN THE PRODUCTION OF REFLEX ACTIONS, *G. Bachman.* *r.s.* Receptive surface; *af.n.* afferent nerve; *e.c.* emissive or motor cells in the anterior horn of the gray matter of the spinal cord, *sp.c.; ef.n.* efferent nerves distributed to responsive organs, *e.g.*, directly to skeletal muscles, *sk.m.*, and indirectly through the intermediation of sympathetic ganglia, *sym.g.*, to blood-vessels, *b.v.*, and to glands, *g.* The nerves distributed to viscera are not represented.

The tonic contraction of the visceral muscles—*e.g.*, the pyloric, the vesical, the anal sphincters—though regarded as automatic by some, is probably reflex in origin, dependent on the arrival of afferent impulses from the periphery. It is probable that future investigation will disclose the existence and pathway of these afferent fibers.

Reflex Excitation.—It has already been stated that the nerve-cells in the spinal cord are capable of receiving and transforming afferent nerve impulses, the result of peripheral stimulation, into efferent nerve impulses, which are reflected outward to skeletal muscles, exciting contraction; to glands, provoking secretion; to blood-vessels, changing their caliber; and to organs, inhibiting or augmenting their activity. All such actions taking place through the spinal cord and medulla oblongata independently of sensation or volition are termed reflex actions. The mechanism involved in every reflex action consists of at least the following structures (Fig. 230):

1. A receptive surface; *e.g.*, skin, mucous membrane, sense organ, etc.
2. An afferent fiber and cell.
3. An emissive cell, from which arises—
4. An efferent nerve, distributed to—
5. A responsive organ, as muscle, gland, blood-vessel, etc.

In this connection the reflex contractions of skeletal muscles only will be considered.

If a stimulus of sufficient intensity be applied to the receptive surface, there will be developed in the terminals of the afferent nerve a series of nerve impulses which will be transmitted by the afferent nerve to, and received by, the dendrites of the emissive cell in the anterior horn of the gray matter. With the reception of these impulses there will be a disturbance in the equilibrium of the molecules of the cells, a liberation of energy, and a transmission of nerve impulses outward through the efferent nerve to the muscle.

A reflex mechanism or arc of this simplicity would subserve but a simple movement. The majority of the reflexes, however, are extremely complex and involve the coöperation and coördination of a number of centers at different levels of the spinal cord and medulla, on the same and opposite sides, and of muscles situated at distances more or less remote from one another. The transference of nerve impulses coming from a localized area of a receptive surface, to emissive cells situated at different levels is accomplished by the intermediation of a third neuron situated in the gray matter, which is in connection, on the one hand, with the central terminals of the afferent nerve and, on the other hand, through collateral branches with the dendrites of the efferent neurons situated at different levels. (Fig. 231.) A histologic and physiologic mechanism of this character readily explains how a localized stimulation can give rise to reflex actions extremely complex in character.

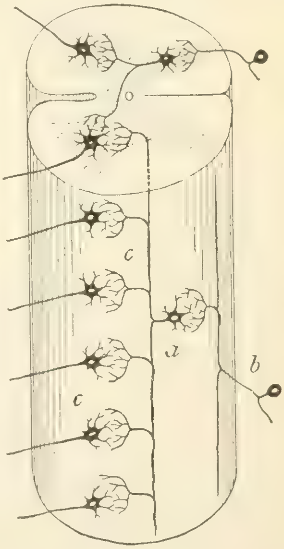

Fig. 231.—Diagram Showing the Relation of the Third Neuron *a*, to the Afferent Neuron *b*, and to the Efferent Neurons *c*, *c*, *c*.—(*After Kölliker.*)

The reflex contractions of skeletal muscles are best studied after division of the central nerve system at the upper limit of the spinal cord. After this procedure the spinal centers can act independently of, and uninfluenced by either sensation or volitional efforts on the part of the animal. Though it is possible to provoke reflex contractions under such circumstances in warm-blooded animals, they are, as a rule, incomplete and of short duration, owing to disturbances of the circulation and respiration and the consequent loss of tissue irritability. In frogs and in cold-blooded animals generally, the spinal cord retains its irritability for a long period of time after removal of the brain, and therefore is well adapted to the study of reflex actions.

The separation of the spinal cord from the brain is readily effected by destroying the medulla oblongata. This can be done by inserting a pin through the skin and the occipito-atlantal membrane covering the space between the occipital bone and the atlas, until it strikes the bodies of the vertebræ below. If the pin is properly directed it passes through the medulla. Care should be taken to avoid injury to the blood-vessels on either side. The brain itself should then be destroyed, so as to remove all consciousness, by inserting the pin into the brain cavity through the foramen magnum, and giving it a few rotatory movements.

A frog so prepared, and placed on the table and allowed to remain at rest for a few moments until the shock of the operation passes away, will draw the limbs close to the body and assume a position not unlike that of a normal frog. If then the posterior limbs be extended, they will immediately be drawn close to the side of the trunk in the usual flexed position. If the toes are pinched with forceps, the foot will execute a series of movements as if the frog were trying to free itself from the source of irritation.

If the frog be suspended, the limbs, through the force of gravity, will be gradually extended and hang down freely. In this, as in the sitting position, the animal will remain perfectly quiet and will not execute spontaneous movements. Any stimulus applied to the skin, however, provided it is of sufficient intensity, will be followed by a more or less pronounced movement. Mechanic, chemic, or electric stimuli applied to any part of the skin will call forth the characteristic reflex movements. Chemic stimuli such as weak solutions of sulphuric or acetic acid placed on the toes will be followed by feeble flexion of the corresponding leg, to be succeeded in a short time by extension. Stronger solutions will produce more extensive and vigorous movements, the foot at the same time being rubbed against the thigh, apparently for the purpose of freeing it from the irritant. Similar phenomena follow the application of the acid to the fingers or the trunk. As a rule, the extent and complexity of the movements is, within limits, proportional to the strength of the stimulus. By limiting the sphere of action of the stimulus to definite but different areas of the skin a great variety of movements, more or less complex and coördinated and apparently purposive and defensive in character, can be produced. The coördinated and purposive character of the movements exhibited by a brainless frog led Pflüger to the assumption that the spinal cord in this as well as in other cold-blooded animals is possessed of sensorial functions, and endowed with rudimentary consciousness. This view, however, is not generally accepted, the movement being attributed to specialized mechanisms in the cord, partially inherited, which permit of one and the same movement with mechanic regularity and precision, so long as the conditions of the experiment remain the same.

In warm-blooded animals similar results may be obtained for a short time after division of the cord, especially if artificial respiration is maintained and the circulation of the blood continued. The cord will then retain its irritability for some time. If the conditions of experimentation were favorable, it is highly probable that the human spinal cord would execute similar movements. Thus it was observed by Robin in a man who had been decapitated that reflex muscle contractions could be elicited by stimulating the skin after the lapse of an hour after execution. "While the right arm was lying extended by the side, with the hand about 25 centimeters distant from the upper part of the thigh, I scratched with the point of a scalpel the skin of the chest at the areola of the nipple, for a space of 10 or 11 centimeters in extent, without making any pressure on the subjacent muscles. We immediately saw a rapid and successive contraction of the great pectoral muscle, the biceps, probably the brachialis anticus, and lastly the muscles covering the internal condyle. The result was a movement by which the whole arm was made to approach the trunk; with rotation inward and half-flexion of the forearm upon the arm; a true defensive movement, which brought the hand toward the chest as far as the pit of the stomach. Neither the thumb, which was partially bent toward the palm of the hand, nor the fingers, which were half bent over the thumb, presented any movements. The arm being replaced in its former position, we saw it again execute a similar movement on scratching the skin, in the same manner as before, a little below the clavicle. This experiment succeeded four times, but each time the movement was less extensive; and at last scratching the skin over the chest produced only contractions in the great pectoral muscle which hardly stirred the limb" (Dalton).

Laws of Reflex Action (Pflüger).

1. *Law of Unilaterality.*—If a feeble irritation be applied to one or more sensory nerves, movement takes place usually on one side only, and that the same side as the irritation.
2. *Law of Symmetry.*—If the irritation becomes sufficiently intense, motor reaction is manifested, in addition, in corresponding muscles of the opposite side of the body.
3. *Law of Intensity.*—Reflex movements are usually more intense on the side of irritation; at times the movements of the opposite side equal them in intensity; but they are usually less pronounced.
4. *Law of Radiation.*—If the excitation still continues to increase, it is propagated upward, and motor reaction takes place through centrifugal nerves coming from segments of the cord higher up.
5. *Law of Generalization.*—When the irritation becomes very intense, it is propagated to the medulla oblongata; motor reaction then becomes general, and it is propagated up and down the cord, so that all the muscles of the body are thrown into action, the medulla oblongata acting as a focus whence radiate all reflex impulses.

Reflex Irritability.—The general irritability or quickness of response of the mechanism involved in reflex action can be approximately determined by observation of the length of time that elapses between the application of a minimal stimulus and the appearance of the muscle response. The method of Türck is sufficiently accurate for general purposes. This consists in suspending a frog, after removal of the brain, and immersing the foot in a 0.2 per cent. solution of sulphuric acid. The time is determined by means of a metronome beating one hundred times a minute. Stimulation of the skin can also be effected by the induced electric current, as suggested by Gaskell. A single shock is, however, ineffective. The currents must follow each other with a rapidity sufficient to give rise to a summation of effects in the nerve-centers which will then be followed by a muscle response. It is highly probably that the chemic stimulation gives rise to a similar summation of effects.

The period of time thus obtained is distributed over the entire mechanism. The true reflex time, however—*i.e.*, the time occupied in the passage of the nerve impulses through the spinal mechanism—is shorter and is obtained by subtracting from the whole period the time occupied by the passage of the impulses through the afferent and efferent nerves as well as the latent period of muscle contraction. This corrected period, the true reflex time, has been found to be twelve times longer than the time occupied by the passage of the nerve impulse through the nerves, including the latent period of the muscle.

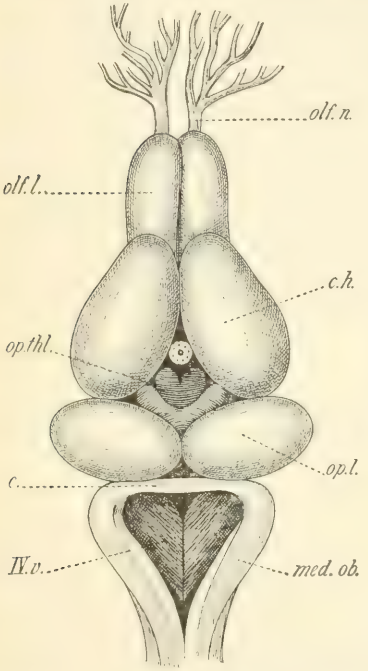

FIG. 232.—DIAGRAM OF THE BRAIN OF THE FROG. *olf. n.* olfactory nerves; *olf. l* olfactory lobes; *c. h.* cerebral hemispheres; *op. thl.* optic thalamus; *op. l.* optic lobes; *c.* cerebellum; *med. ob.* medulla oblongata; *IV. v.* fourth ventricle.

The total reflex time, that is, the time elapsing between the application of the stimulus and the response of an organ may be *shortened* by influences which heighten the irritability of any one or more portions of the reflex arc: *e.g.*

1. *Separation of the Brain from the Cord.*—This is at once followed by an increase in reflex irritability, and is taken as evidence that the brain is normally exerting an inhibitor influence over the reflex centers of the cord. The same increase is observed upon hemisection of the cord, though the increase is limited to the same side.
2. *The Toxic Action of Drugs.*—Many drugs increase the irritability of the spinal cord, though the most efficient is strychnin. This drug, even in small doses, increases the irritability to such an extent that a minimal stimulus is sufficient to call forth spasmodic contractions of all the skeletal muscles. Under its influence the usual coördinated reflexes disappear and are succeeded by incoördinated reflexes. The explanation of this fact is believed to be a diminution in the resistance offered by the cord to the passage of the afferent impulses rather than to a direct stimulation of the efferent cells. So much is this resistance decreased that the nerve impulses instead of being confined to their accustomed paths, are radiated in all directions. Absolute repose of the animal and the exclusion of all external stimuli greatly diminish the tendency to the occurrence of spasms.
3. *Degeneration of the Pyramidal Tracts.*—In primary lateral sclerosis, a pathologic condition characterized primarily by a degeneration of the terminal filaments of the pyramidal tract fibers, the reflex activity of

the cord becomes exalted. As the disease progresses the irritability increases to such an extent that violent spasmodic contractions of the arms and legs arise when the skin or tendons are mechanically stimulated. The explanation offered is practically the same as in division of the cord: viz., withdrawal of the inhibitor and controlling influence of the brain.

The total reflex time may be lengthened by influences which lower the irritability of any one or more portions of the reflex arches.

1. *Stimulation of Certain Regions of the Brain.*—It was discovered by Setchenow that when the frog brain is divided just anterior to the optic lobes (Fig. 232) and the reflex time subsequently determined according to the method of Türck, the time can be considerably lengthened by stimulation of the optic lobes. This is readily accomplished by placing small crystals of sodium chlorid on the optic lobes. It was concluded from this fact that these lobes contain centers which exert an inhibitor influence over centers in the spinal cord through descending nerve-fibers. This conclusion is strengthened by the fact that division of the brain just behind the optic lobes causes a temporary inhibition of the reflexes in consequence of a mechanical irritation of these fibers. It is quite probable that the volitional inhibition of certain reflexes is accomplished through the intermediation of this center localized by Setchenow.
2. *Stimulation of Sensor Nerves.*—If during the application of a stimulus sufficient to call forth a characteristic reaction in a definite period of time, a sensor nerve in a distant region of the body be simultaneously stimulated, it will be found that the reflex time will be lengthened or the reaction completely inhibited.
3. *Lesions of the Spinal Cord; e.g.*, atrophy of the multipolar cells of the anterior horns of the gray matter; degeneration of the terminals of the dorsal root-fibers.
4. *The Toxic Action of Drugs—e.g.*, chloroform, chloral—which are believed to exert a depressing action on the nerve-cells themselves.

Special Reflex Actions.—Among the reflexes connected with the more superficial portions of the body there are some which are so frequently either increased or diminished in pathologic conditions of the spinal cord that their study affords valuable indications as to the seat and character of the lesions. They may be divided into:

1. The skin or superficial reflexes.
2. The tendon or deep reflexes.
3. The organ reflexes.

The skin reflexes, characterized by contraction of underlying muscles, are induced by stimulation of the afferent nerve-endings of the skin—*e.g.*, by pricking, pinching, scratching, etc. The following are the principal skin reflexes:

1. *Plantar reflex*, consisting of contraction of the muscles of the foot, induced by stimulation of the sole of the foot; it takes place through the segments of the cord which give rise to the second and third sacral nerves.
2. *Gluteal reflex*, consisting of contraction of the glutei muscles when the skin over the buttock is stimulated; it takes place through the segments giving origin to the fourth and fifth lumbar nerves.
3. *Cremasteric reflex*, consisting of a contraction of the cremaster muscle

and a retraction of the testicle toward the abdominal ring when the skin on the inner side of the thigh is stimulated; it takes place through the segments which give origin to the first and second lumbar nerves.

4. *Abdominal reflex*, consisting of a contraction of the abdominal muscles when the skin upon the side of the abdomen is gently scratched; it takes place through the spinal segments which give origin to the nerves from the eighth to the twelfth thoracic.
5. *Epigastric reflex*, consisting of a slight muscular contraction in the neighborhood of the epigastrium when the skin between the fourth and sixth ribs is stimulated; it takes place through the segments of the cord which give origin to the nerves from the fourth to the seventh thoracic inclusive.
6. *Scapular reflex* consisting of a contraction of the scapular muscles when the skin between the scapulæ is stimulated; it takes place through the segments of the cord which give rise to the nerves from the fifth cervical to the third thoracic inclusive.

The skin or superficial reflexes, though variable, are generally present in health. They are increased or exaggerated when the gray matter of the cord is abnormally excited, as in tetanus, strychnin-poisoning, and disease of the lateral columns.

The so-called "*tendon reflexes*," are characterized by a movement of certain parts of the body due to the contraction of certain muscles and are elicited by a sharp tap on their tendons. The fundamental condition for the production of the tendon reflex is a certain degree of tonus of the muscle, which is a true reflex, maintained by afferent nerve impulses developed in the muscle itself in consequence of its extension and hence compression of the end-organs, the muscle spindles, of the afferent nerves. When the muscle is passively extended, as it must be when the reflex is to be elicited, there is an exaltation of the tonus and an increase in the irritability. To this condition of the muscle due to passive tension, the term myotatic irritability has been given. If the muscle extension be now suddenly increased, as it is when the tendon is sharply tapped, the increased compression of the muscle spindles will develop additional afferent impulses which after transmission to the spinal cord will give rise to contraction of the corresponding muscle. The tendon reflexes are of much value in the diagnosis of certain lesions of the spinal cord.

The following are the principal forms of the tendon reflexes:

1. *The Patellar tendon reflex or knee-jerk.* This phenomenon is characterized by a quick extension of the leg from the knee downward, due to the contraction of the extensor muscles of the thigh, when the ligamentum patellæ is struck between the patella and tibia. This reflex is best observed when the legs are freely hanging over the edge of a table. The patella reflex is generally present in health, being absent in only 2 per cent.; it is greatly exaggerated in lateral sclerosis, in descending degeneration of the cord; it is absent in locomotor ataxia and in atrophic lesions of the anterior gray cornua.
2. *The tendo-Achillis reflex or ankle-jerk.* This phenomenon is characterized by a flexion of the foot due to a contraction of the gastrocnemius muscle when the tendo-Achillis is struck. To elicit the contraction, the leg should be extended and the dorsum of the foot be pressed toward the

leg so as to give to the gastrocnemius a slight degree of extension. If the tendon be now sharply struck a quick flexion of the foot is produced.

3. *Ankle clonus.*—This phenomenon consists of a series of rhythmic contractions of the gastrocnemius muscle, varying in frequency from six to ten per second. To elicit this reflex, pressure is made upon the sole of the foot so as to extend the foot at the ankle suddenly and energetically, thus putting the tendo-Achillis and the gastrocnemius muscle on the stretch. The rhythmic movements thus produced continue so long as the tension within limits is maintained. Ankle clonus is never present in health, but is very marked in lateral sclerosis of the cord.
4. *The Toe Reflex.*—This phenomenon is characterized by a flexion of the foot, then of the leg and perhaps of the thigh when the great toe is strongly and suddenly flexed. It is present in those diseases of the spinal cord in which there is a pronounced patellar reflex.
5. *The Wrist and Elbow Reflex.*—These phenomena are characterized by an extension movement of the hand and arm when the tendons of the extensor muscles are sharply tapped. These reflexes are especially marked in primary lateral sclerosis of the cord in the upper portion.

The *organ reflexes*, *e.g.*, the activities of the genito-urinary organs, the stomach, intestines, gall-bladder, etc., which are induced by peripheral stimulation have been considered in connection with the physiologic action of these organs. The genito-urinary center is located in the lumbar region of the spinal cord. In diseased conditions of this region the genito-urinary reflexes are sometimes increased, at other times decreased or even abolished.

Direct or Cerebral Excitation.—The activity of the emissive cells of the spinal cord segments, due to the arrival of nerve impulses descending the spinal cord from the cerebrum, in consequence of psychic states of a volitional or of an affective or emotional character, will be considered in a subsequent paragraph entitled "encephalo-spinal conduction."

B. THE SPINAL CORD SEGMENTS AS CONDUCTORS.

The white matter of the spinal cord consists of nerve-fibers the special functions of which are

1. To conduct nerve impulses from one segment of the cord to another.
2. To conduct nerve impulses coming to the cord through afferent nerves, directly or indirectly to various areas of the encephalon.
3. To conduct nerve impulses from the encephalon to the spinal cord segments.

Intersegmental or Associative Conduction.—The spinal cord consists of a series of physiologic segments each of which has specific functions and is associated through its related spinal nerve with a definite segment of the body. For the harmonious coöperation and coördination of all the spinal segments it is essential that they should be united by commissural or associative fibers. This is, in fact, accomplished by the axons of the intrinsic cells of the gray matter, which constitute such a large part of the antero-lateral and posterior root zones. In consequence of this association, the cord becomes capable of complex coördinated and purposive reflex actions.

Some of the nerve-fibers arising in the intrinsic cells become associated with the cerebellum through the direct cerebellar tract and the antero-lateral cerebellar tract. By this means the cord and cerebellum are associated in functional activity.

Spino-encephalic or Sensor Conduction.—The spino-encephalic or sensor pathway extends from different levels of the spinal cord to the cortex of the cerebrum, and consists of two or more consecutively arranged groups of neurons. The first group of these neurons extends from the spinal cord to the thalamus and is known as the *spino-thalamic* system; the second group of these neurons extends from the thalamus to the cortex of the cerebrum and is known as the *thalamo-cortical* system.

The spino-thalamic system is connected with the cutaneous and mucous surfaces, and with the tendons, joints and muscles by means of the dorsal root fibers of the spinal nerves. Histologic and clinical investigations have shown that the central terminations of the nerve-fibers coming from the skin, become associated with afferent cells on the same side of the gray matter, at the same or at somewhat different levels; that the axons of these cells cross the median plane and then pass upward through the cord, medulla, pons and crura cerebri to the thalamus. Similar methods of investigation have shown that the nerve-fibers coming from the tendons, joints, and muscles ascend the white matter of the spinal cord of the same side, as far as the upper limits of the posterior column, where their terminal branches become associated with the cells of the cuneate and gracile nuclei. From the cells of these nuclei, axons arise which cross the middle plane of the medulla to join the fibers ascending the spinal cord. The former fibers are known as the internal arcuate fibers and assist in the formation of the *lemniscus* or *fillet* (Fig. 233). The afferent or sensor pathway thus decussates in part, at different levels of the spinal cord, and in part at the level of the gracile and cuneate nuclei. The former is often termed the lower, the latter the upper sensor decussation or crossway.

The afferent pathway on passing toward the thalamus receives additional fibers at the level of the medulla and pons from the cells of the opposite side with which the terminations of the afferent cranial nerves, the trigeminal, glossopharyngeal, and vagus, are associated.

The nerve impulses that arise in consequence of impressions made on the terminals of the nerves in the cutaneous and mucous surfaces, in the viscera and in the muscles, are transmitted through the dorsal roots of the spinal nerves to the cord. On reaching the cord the cutaneous nerve impulses are received by afferent or receptive nerve-cells in the gray matter, and transmitted by their axons across the median plane of the spinal cord and then upward to and through the medulla, the posterior part of the pons, the posterior part of the crura cerebri, and for the most part to the ventral portion of the thalamus opticus.

On reaching the thalamus the nerve impulses are received by nerve-cells, and then transmitted by their axons which pass by way of the internal capsule to the cells of the cortex of the cerebrum. It is probable however that some fibers from the cord and medulla pass direct to the cortex. When thus transmitted through the cord to the cerebral hemispheres directly or indirectly, they are received by specialized nerve-cells in the cortex and translated into conscious sensations. The nerve impulses developed in tendons and muscles are received by localized groups of nerve-cells, the nucleus gracilis and nucleus cuneatus, situated at the top of the posterior column, which are reached by the upward coursing of some of the dorsal root fibers through the columns of Goll and Burdach. They are then transmitted by the internal arcuate fibers and the fillet either directly or indirectly to the cortex of the cerebrum and translated into conscious sensations. The sensations thus arising may be divided into special and general sensations. Of the former may be mentioned the sensations of temperature, pain, touch, pressure, passive position and movements of parts due to the activity of skeletal muscles; of the latter may be mentioned hunger, thirst, fatigue, well-being, etc.

Though all the impulses that give rise to these varied sensations are contained within the fibers of the afferent peripheral nerves, they are on reaching the cord distributed by the intraspinal mechanisms to different tracts of nerve-fibers, each of which transmits to localized areas of the cerebral cortex, the *somesthetic* areas, a special group of impulses which give rise to sensations of various kinds such as those just mentioned.

The current views regarding the physiologic activities of the afferent portion of the peripheral nerve system and its relation to the production of different forms of sensibility have been enlarged by the results of the investigations that have been made by Head. Thus, he has shown that the afferent nerves consist of three systems, each of which when excited to activity evokes in consciousness a different and distinct group of sensations as follows:

1. One system of nerves which when stimulated evoke sensations through which is gained the power of cutaneous localization, of the discrimination of two points of a compass, of the finer grades of temperature, and of light touch. To this form of cutaneous sensibility the term *epicritic* has been applied.
2. A second system of nerves which when vigorously stimulated, as by the prick of a pin or by the application of a hot or cold object, evoke sensations of pain or heat and cold. To this form of cutaneous sensibility the term *protopathic* has been applied. This form of sensibility is unaccompanied by a definite appreciation of the locality stimulated for the reason that the stimulus causes a widespread or radiating sensation which at times is referred to parts far removed from the part stimulated.
3. A third system of nerves which when stimulated evoke sensations of pressure, of the passive position and the movements of parts of the body, and sensations of pain as well, if the stimulus (pressure) be severe, or if the underlying structures are injured, *e.g.*, the rupture of a joint. The nerves subserving this form of sensibility are contained in the trunks of the motor (muscle) nerves and are distributed to muscles, tendons and joints. To this form of sensibility the term *deep* has been applied.

The pathways through the spinal cord that conduct these afferent impulses to the brain are ill-defined and imperfectly known, and only for a few sensations can it be said that their pathways have been determined. The reason for this obscurity lies partly in the difficulties of experimentation, partly in the difficulties of interpretation. Clinical observations are for special reasons more or less untrustworthy.

As the outcome of many investigations it may be said that a transverse section of one lateral half of the cord in the monkey, or a lesion involving the one lateral half in man, as a rule abolishes many if not all forms of cutaneous sensibility on the opposite side below the injury. This would seem to prove that the nerve impulses cross the median line of the cord immediately or very shortly after entering and then ascend the corresponding half of the cord on their way to the thalamus. At the same time, muscle sensibility is abolished on the same below the injury. This would seem to prove that the fibers of the posterior roots that enter and cross the column of Burdach and ascend in the column of Goll to terminate around the cells of the gracile and cuneate nuclei are derived mainly from the muscles.

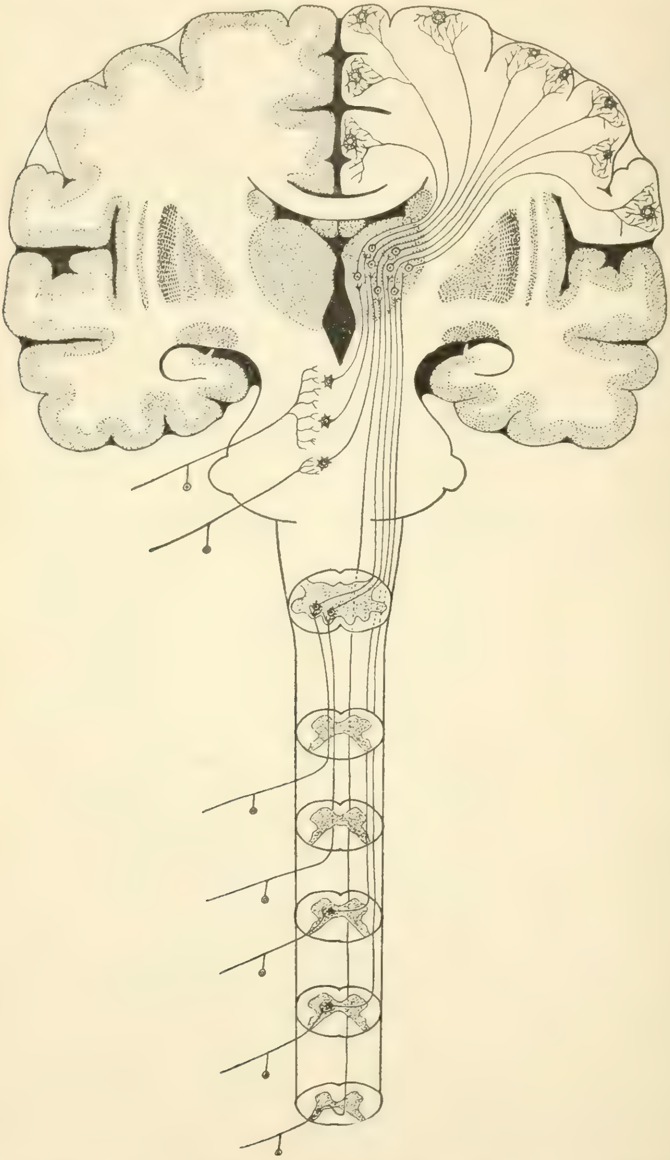

FIG. 233.—DIAGRAM OF THE SENSOR PATHWAYS IN THE SPINAL CORD ENLARGED ABOVE BY FIBERS OF THE SENSOR CRANIAL NERVES AND NERVES OF SPECIAL SENSE.

It is, however, believed by some investigators that those fibers which subserve the sense of touch do not decussate at once, but ascend in the column of Goll as far as the medulla oblongata, where they, in common with the fibers coming from the muscles, arborize around the nerve-cells in the gracile and cuneate nuclei.

The pathways for the impulses that give rise to the different sensation have been variously located by different observers, *e.g.*, in the gray matter, in the limiting layer, and in the antero-lateral tract of Gowers; the pathway for the impulses that give rise to temperature sensations has been located in the gray matter; the pathway for tactile impressions has been located in the posterior columns, though this is not beyond dispute. The pathway for pain sensations has been located in Gowers' tract.

The results on both sides of the body, which follow a transverse lesion, experimental or traumatic, of one-half of the spinal cord in the thoracic region for example, are shown in the subjoined table, a grouping of results which is known as the Brown-Séquard "Symptom Complex." It is understood, of course, that these results are observed below the level of the lesion.

THE BROWN-SÉQUARD SYMPTOM COMPLEX

Side Opposite of Lesion.	Side of Lesion.
1. Temperature sensibilities abolished.	1. Temperature sensibilities retained.
2. Painful sensibilities abolished.	2. Painful sensibility retained.
3. Pressure (painful) sensibilities abolished.	3. Pressure (painful) sensibilities retained.
4. Passive position of limb and direction of movement, retained.	4. Passive position of limb and direction of movement, abolished.
5. Light pressure or light touch, may or may not be abolished.	5. Light pressure or light touch, retained.
6. Tactile discrimination, retained.	6. Tactile discrimination, abolished.
7. Cutaneous localization, abolished.	7. Cutaneous localization, retained.
8. Voluntary motion, retained.	8. Voluntary motion, abolished.

From a study of this table it is apparent: (1) that some forms of sensor impulses (those of pain and temperature sensibility) cross soon after their entrance and pass up the opposite side of the cord; (2) that other forms of sensor impulses (those of the sense of passive position of a limb and of the direction of movement and tactile discrimination (Head)) do not cross, but pass up on the same side as the entering dorsal nerve roots; (3) that tactile sensibility may or may not be abolished on the side opposite the lesion; and (4) that the sense of cutaneous localization may be dissociated from the sense of passive position, and remain intact when the latter is absent (Head).

Encephalo-spinal or Motor Conduction.—The encephalo-spinal or motor pathway extends from the cerebral cortex to different levels of the gray matter of the aqueduct of Sylvius, of the pons, medulla and spinal cord. It is connected at these different levels with the efferent nerve-cells which give origin to the nerve-fibers which collectively constitute the cranial or encephalic motor nerves and the ventral spinal nerves all of which are distributed to skeletal muscles.

The reason for the development of this pathway is apparent from the following considerations:

At birth the child is capable of performing all the functions of organic life, such as sucking, swallowing, breathing, etc. It is, however, deficient in psychic activity and in volitional control of its muscles. Its movements are therefore largely, if not entirely, reflex in character.

Embryologic and histologic examination of the spinal cord and medulla show that so far as their mechanisms for independent physiologic activities are concerned both are fully developed. Similar investigations of the cerebral hemispheres and of the nerve-fibers which bring their nerve-cells into relation with the spinal segments show that the cells of the cortex are not only immature, but that their descending axons are incompletely invested with myelin. With the growth of the child, psychic life unfolds and volitional control of muscles is acquired. Coincidently the cells of the cerebral cortex grow and develop and the fibers become covered with myelin.

The nerve-fibers, which have their origin in the cells of the cerebral cortex, and which terminate in tufts around the cells in the anterior horns of the gray matter of the spinal segments, are to be regarded as long commissural tracts uniting and associating these two portions of the central nerve system.

Experimental investigations and observations of pathologic lesions accord with the view that physiologically these fibers are efferent pathways for the transmission of motor or volitional impulses from the cortex to the spinal segments. The nerve-cells in which the motor impulses originate are located for the most part, as will be fully stated later, in the central portion of the cortex of the cerebral hemispheres in the neighborhood of the central or Rolandic fissure. The axons of these cells from each hemisphere descend through the corona radiata to and through the internal capsule, along the inferior surface of the crura cerebri, behind the pons to the medulla, of which they constitute the anterior pyramids (Fig. 234). At this point the pyramidal tract[1] of each side divides into two portions, viz.:

1. A large portion, containing from 80 to 90 per cent. of the fibers, which decussates at the lower border of the medulla and passes downward in the posterior part of the lateral column of the opposite side, constituting the *crossed pyramidal tract;* as it descends it gradually diminishes in size as its fibers or their collaterals enter the gray matter of each successive segment.
2. A small portion, containing from 20 to 10 per cent. of the fibers, which does not decussate at the medulla but passes downward on the inner side of the anterior column of the same side, constituting the *direct pyramidal tract* or column Türck. This tract can be traced down, as a rule, only as far as the mid-dorsal region. As it descends it becomes smaller as its fibers cross the anterior commissure to enter the gray matter of the opposite side. Thus all the fibers of the pyramidal tract from each cerebral hemisphere eventually are brought into relation with the cells of the gray matter of the opposite side of the cord.

[1] From the fact that the region included between the origin of these fibers and the internal capsule presents somewhat the form of a pyramid with four sides, Charcot designated it the pyramidal region and the fibers composing it the *pyramidal tract*. The base of the pyramid includes the convolutions of the cortex in front of the Rolandic fissure. The summit of the pyramid is truncated and covers the *pyramidal* region of the internal capsule.

That the pyramidal tracts are the conductors of volitional impulses throughout the length of the cord to its various segments has been made

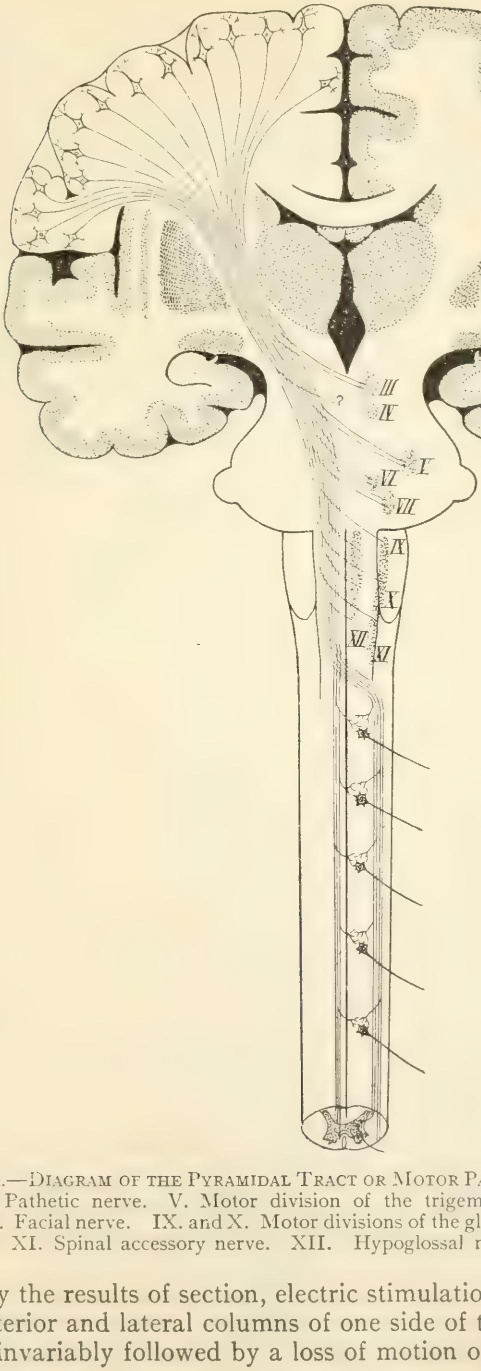

FIG. 234.—DIAGRAM OF THE PYRAMIDAL TRACT OR MOTOR PATH. III. Common oculo-motor nerve. IV. Pathetic nerve. V. Motor division of the trigeminal nerve. VI. The abducens nerve. VII. Facial nerve. IX. and X. Motor divisions of the glosso-pharyngeal and pneumogastric nerves. XI. Spinal accessory nerve. XII. Hypoglossal nerve.—(*Van Gehuchten.*)

evident by the results of section, electric stimulation, and disease. Division of the anterior and lateral columns of one side of the cord in any part of its extent is invariably followed by a loss of motion or paralysis of the muscles below the section, while electric stimulation of the peripheral end of the isolated crossed pyramidal tract is followed by marked characteristic movements of the muscles. Similar results follow division of the pyramidal tract in any part of its course from the cerebral cortex downward. Electric stimulation of the cortical cells which give origin to the pyramidal tract is also followed by contraction of the muscles of the opposite side, while their destruction is attended by paralysis of the same muscles. As the nutrition of the fibers is governed by the cells, it follows that when the axon is separated from its cell-body it degenerates. It has been found that a lesion of the pyramidal tract in any part of its course is followed by descending degeneration, which is taken in evidence that it conducts nerve impulses from above downward. Thus experimental investigation and pathologic observation are in accord in the view that physiologically these nerve-fibers are the pathways for the transmission of motor or volitional impulses from the encephalon to the spinal cord.

The pyramidal tracts are also the conductors of the nerve impulses discharged by the cells of the cerebrum during the occurrence of the affective or emotional states, that excite to activity the lower nerve centers; those that give origin to the autonomic nerve fibers which excite to activity the epithelium of glands, the non-striated muscles in the walls of the blood-vessels and viscera.

CHAPTER XXII

THE ANATOMIC RELATIONS OF THE MEDULLA OBLONGATA; THE ISTHMUS OF THE ENCEPHALON; THE CORPORA QUADRIGEMINA; THE BASAL GANGLIA

THE MEDULLA OBLONGATA

The **medulla oblongata** is that portion of the central nerve system immediately superior to and continuous with the spinal cord. It has the shape of a truncated cone, the base of which is directed upward, the truncated apex downward. It is 38 mm. in length, 18 mm. in breadth, and 12 mm. in thickness. By the continuation upward of the anterior and posterior median fissures, the medulla is divided into symmetric halves (Figs. 235 and 236). Like the cord, of which it is a continuation, it is composed of white matter externally and gray matter internally.

Structure of the Gray Matter.—The gray matter of the medulla is continuous with that of the cord, though owing to the shifting of position of the different tracts of the white matter it is arranged with much less regularity. The appearance which the gray matter presents on transverse section varies also at different levels.

At the level of the first cervical nerve the posterior horns are narrow, elongated, and directed outward. The lateral horns are well developed and present a collection of cells near their bases which can be traced upward and downward for some distance. At the level of the decussation of the pyramidal tracts the head of the anterior horn becomes detached from the rest of the gray matter and is pushed backward toward the posterior horn; the bases of the anterior horns become spread out to form a layer of gray matter near the dorsal aspect of the medulla. Transverse sections of the medulla at all levels show a more or less extensive network of nerve-fibers known as the *reticular formation*. In its meshes are found collections of nerve-cells of varying size. Toward the dorsal aspect of the medulla special groups of cells are found from which axons arise to become the fibers of various efferent cranial nerves, *e.g.*, hypoglossal, efferent fibers of the vagus, and glossopharyngeal.

Structure of the White Matter.—The white matter is composed of nerve-fibers supported by connective tissue and neuroglia. It is subdivided on either side by grooves into three main columns: viz., an anterior column or pyramid, a lateral column, and a posterior column.

The *anterior column* or pyramid is composed partly of fibers continuous with those of the anterior column of the spinal cord (the direct pyramidal tract), and partly of fibers continuous with those of the lateral column of the cord of the opposite side (the crossed pyramidal tract), which decussate at the anterior portion of the medulla. The united fibers can be traced upward to the pons, where they disappear from view.

The *lateral column* is composed of fibers continuous with those of the lateral column of the cord. As the fibers pass upward, however, they diverge in several directions. The fibers of the crossed pyramidal tract cross the median line, as previously stated, to enter into the formation of the anterior column; the fibers of the direct cerebellar tract gradually curve backward, and in so doing unite with other fibers to form the restiform body, after which they enter the cerebellum by way of the inferior peduncle. Situated between the anterior pyramid and the restiform body is a small oval mass, the olivary body, composed of both white and gray matter.

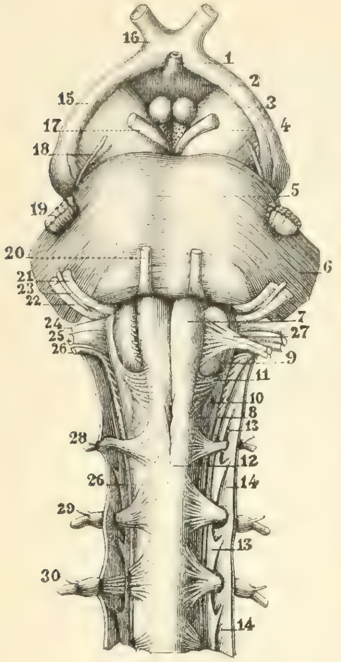

FIG. 235.—ANTERIOR OR VENTRAL VIEW OF THE MEDULLA OBLONGATA AND ISTHMUS. 1. Infundibulum. 2. Tuber cinereum. 3. Corpora albicantia. 4. Cerebral peduncle. 5. Tuber annulare. 6. Origin of the middle peduncle of the cerebellum. 7. Anterior pyramids of the medulla oblongata. 8. Decussation of the anterior pyramids. 9. Olivary bodies. 10. Restiform bodies. 11. Arciform fibers. 12. Upper extremity of the spinal cord. 13. Ligamentum denticulatum. 14, 14. Dura mater of the cord. 15. Optic tracts. 16. Chiasm of the optic nerves. 17. Motor oculi communis. 18. Patheticus. 19. Fifth nerve. 20. Motor oculi externus. 21. Facial nerve. 22. Auditory nerve. 23. Nerve of Wrisberg. 24. Glosso-pharyngeal nerve. 25. Pneumogastric. 26, 26. Spinal accessory. 27. Sublingual nerve. 28, 29, 30. Cervical nerves.—(*Sappey.*)

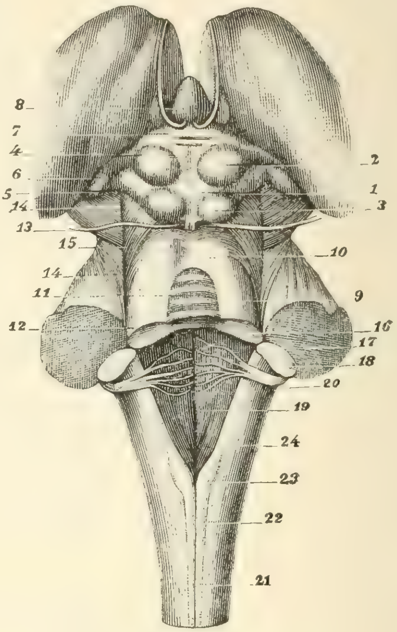

FIG. 236.—POSTERIOR OR DORSAL VIEW OF THE MEDULLA OBLONGATA, ISTHMUS, AND BASAL GANGLIA. 1. Corpora quadrigemina. 2. Corpus quadrigeminum anterius (pregeminum). 3. Corpus quadrigeminum posterius (post-geminum). 4. Tract of fibers (brachium) passing to the corpus geniculatum externum. 5. Tract of fibers (brachium) passing to 6, the corpus geniculatum internum. 7. Posterior commissure. 8. Pineal gland. 9. Superior cerebellar peduncle. 10, 11, 12. The valve of Vieussens. 13. The pathetic nerve. 14. Lateral groove of the isthmus. 15. Triangular bundle of the isthmus. 16. Superior cerebellar peduncle. 17. Middle cerebellar peduncle. 18. Inferior cerebellar peduncle. 19. Antero-inferior wall of the fourth ventricle. 20. Acoustic nerve. 21. Spinal cord. 22. The postero-median column. 23. The posterior pyramids.—(*Sappey.*)

The *posterior column* is composed largely of fibers continuous with those of the posterior column of the cord. The subdivision of this column into a postero-external (Burdach) and a postero-internal (Goll) is more marked in the medulla than in the cord. The former is here known as the *funiculus cuneatus*, the latter as the *funiculus gracilis*. These two strands of fibers are apparently continued into the restiform body. Owing to the divergence of the restiform bodies a V-shaped space is formed, the floor of which is covered with epithelium resting on the ependyma. At the upper extremity of the funiculus cuneatus and funiculus gracilis, two collections of gray matter are found, known respectively as the *nucleus cuneatus* and *nucleus gracilis*. Around the cells of these nuclei many of the fibers of the posterior column end in brush-like expansions (see Fig. 233).

The Fillet or Lemniscus.—From the ventral surface of the cuneate and gracile nuclei axons emerge which pass forward and upward through the gray matter and decussate with corresponding fibers coming from the opposite nuclei. They then assume a position just posterior to the pyramids and between the olivary bodies. These fibers thus form a new tract, termed the fillet or lemniscus. As this tract ascends toward the cerebrum it receives additional axons from the sensor end-nuclei of all the afferent cranial nerves of the opposite side with the exception of the auditory. From the end-nuclei of the auditory nerve, new axons ascend as a distinct tract situated near the lateral aspect of the pons. From their position, these two separate tracts have been termed the *mesial* and *lateral* fillets respectively.

THE ISTHMUS OF THE ENCEPHALON

The **isthmus of the encephalon** comprises that portion of the central nerve system connecting the cerebrum above, the cerebellum behind, and the medulla below. Its *ventral surface* presents below an enlargement, convex from side to side, the *pons Varolii*. On each side the fibers of which the pons consists converge to form a compact bundle, the middle peduncle, which enters the corresponding half of the cerebellum. Above the pons, this surface presents two large columns of white matter which diverge somewhat from below upward, enter the base of the cerebrum and are known as *crura cerebri*. Embracing the crura above are two large bands of white matter, the optic tracts (Fig. 235).

The *dorsal surface* presents below two diverging columns of white matter, the inferior peduncles; above, two converging columns, the superior peduncles of the cerebellum (Fig. 236). At the extreme upper part of this surface there are four small grayish eminences, the *corpora quadrigemina*. From the disposition of the white matter on the dorsal surface of the isthmus and medulla, there is formed a lozenge-shaped space, the *fourth ventricle*. The space is an expansion of the central cavity of the cord, the result of the changed relations of the white and gray matter in this region of the central nerve system. Above, this ventricle communicates by a narrow canal, the aqueduct of Sylvius, with the third ventricle. The floor of the fourth ventricle is covered with a layer of epithelium resting on the ependyma continuous with that lining the central canal of the cord. Beneath this is a layer of gray matter.

The **pons varolii** comprises in a general way that portion of the central nerve system situated between the medulla oblongata and the crura cerebri. The ventral surface is convex from side to side; the lateral surface, owing to the convergence of the fibers of which it is composed, is contracted to form the middle peduncle of the cerebellum; the posterior surface is flat and forms the upper half of the floor of the fourth ventricle. The pons consists of white fibers and gray matter supported by connective tissue and neuroglia. Transverse sections of the pons show that it is divided into an *anterior* or *ventral*, and a *posterior* or *dorsal portion*, the latter being usually termed the tegmentum.

The *ventral portion* consists for the most part of white fibers, arranged longitudinally and transversely (Fig. 237). The longitudinal fibers are largely continuations of the pyramidal tracts, or the fibers composing in part the anterior pyramid of the medulla. In the lower part of the pons these fibers are compactly arranged, but at higher levels they are separated into a number of bundles by the interlacing of the transverse fibers. The transverse fibers are divided into a superficial and a deep set. Among these fibers are groups of nerve-cells which collectively are known as the *nucleus pontis*. Some of the transverse fibers, especially the superficial ones, are commissural in character—*i.e.*, they connect corresponding parts of the gray matter of the lateral halves of the cerebellum; others coming from the gray matter of the cerebellum cross the median line and terminate around the cells of the nucleus pontis; others again are connected with the gray cells of the same side. Through the intermediation of the nucleus pontis and certain of the longitudinal fibers of the pons, the cerebellum is brought into relation with the cerebrum.

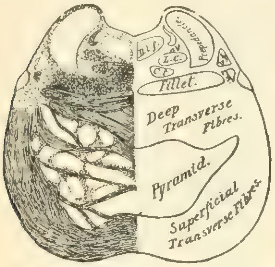

FIG. 237.—TRANSECTION OF THE PONS THROUGH ITS MIDDLE PORTION, SHOWING THE RELATION OF THE NERVE TRACTS OF WHICH IT IS COMPOSED. *D. l. f.* Dorsal longitudinal fasciculus. *L.c.* and *c.* Locus ceruleus. *L.f.* Lateral fillet.

The *dorsal* or *tegmental portion* consists of: (1) The fillet; (2) the formatio reticularis; (3) the medial longitudinal bundle; (4) groups of efferent and afferent nerve-cells.

The *fillet* or *lemniscus* in this region is divided into a mesial and a lateral portion. The fibers of the *mesial portion* are partly the axons of the nerve-cells of the gracile and cuneate nuclei of the opposite side of the medulla, and partly of the axons of the sensor nerve-cells of the afferent cranial nerves with the exception of the auditory. The fibers of the *lateral portion* are mainly the axons of the cells in the floor of the fourth ventricle around which the auditory nerve-fibers end. They are therefore a continuation of the *acoustic tract*.

The *formatio reticularis* is a continuation of that of the medulla.

The *medial longitudinal bundle* is a band of nerve-fibers, triangular in shape, placed on either side of the median line just beneath the floor of the fourth ventricle and the aqueduct of Sylvius. It consists of both afferent (ascending) and efferent (descending) fibers. The *afferent* fibers are the axons of sensor end-nuclei located in the upper segments of the spinal cord as well as of axons of sensor end-nuclei of cranial nerves. As they pass upward some of the fibers, as well as collateral branches, arborize around the nuclei of origin of the various motor cranial nerves of the same and opposite sides. The ascending fibers thus associate anatomically sensor end-nuclei of both spinal and cranial nerves with the nuclei of the motor cranial nerves. The *efferent* fibers are the axons of nerve-cells located in the corpora quadrigemina and in a special nucleus in the floor of the third ventricle. From this origin the fibers soon cross the median line, pursue a downward course and come into close relation with the ascending fibers. In their descent fibers pass successively to the nuclei of origin of the motor cranial nerves and to nuclei in the upper segments of the spinal cord. The efferent fibers thus associate anatomically the nuclei from which they arise with the nuclei just alluded to.

The *superior olive* is a cylindric mass of gray matter situated in the pons in the anterior part of the formatio reticularis. It consists of nerve-cells the axons of which pass dorso-laterally, decussate in the median line, and form the lateral fillet of the opposite side. Some few axons go to the lateral fillet of the same side.

The groups of efferent nerve-cells lying just beneath the floor of the fourth ventricle give origin to axons composing the motor portion of the fifth, the sixth, the seventh cranial nerves. The groups of afferent cells are the sensor end-nuclei of the fifth and eighth cranial nerves from which new axons pass as a part of the mesial and lateral fillets toward the cerebrum.

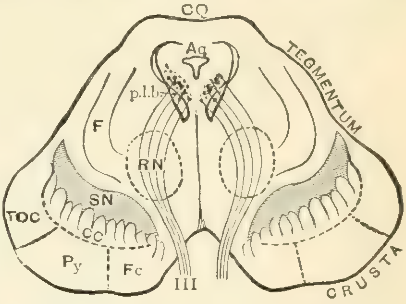

Fig. 238.—Scheme of Transverse Section of the Cerebral Peduncles. CQ. Corpora quadrigemina. Aq. Aqueduct. p.l.b. Posterior longitudinal bundle. F. Fillet or lemniscus. RN. Red nucleus. SN. Substantia nigra. III. Third nerve. Py. Pyramidal tracts. Fc. Fronto-cerebellar; and TOC, temporo-occipital fibers of the crusta. CC. Caudato-cerebellar fibers in upper part of crusta.—(*After Wernicke and Gowers.*)

The **crura cerebri** comprise that portion of the central nerve system situated between the pons below and the cerebrum above. They are composed of strands of nerve-fibers which are divided, as shown on cross-section, into a *ventral* and a *dorsal* portion by a crescentic-shaped layer of gray matter, the substantia nigra (Fig. 238). Of the fibers which compose the *ventral portion* of each crus, the *crusta or pes*, the larger part is continuous below, through the longitudinal fibers of the pons, with the pyramid of the medulla and the pyramidal tract; above they assist in the formation of the internal capsule. On the inner and on the outer side of each crusta there is a bundle of fibers derived from the frontal, and from the temporal and occipital portions of the cerebrum respectively. These fibers are connected directly with the nuclei pontis and indirectly with the cerebellum of the same and opposite sides. The fibers which compose the *dorsal portion*, the ***tegmentum***, are continuous with those which pass upward from the medulla and pons, *e.g.*, the fillet, both mesial and lateral, the formatio reticularis, the medial longitudinal bundle, and, in addition, the fibers of the superior peduncles of the cerebellum. Above, the fibers terminate largely in collections of gray matter at the base of the cerebrum.

The *aqueduct of Sylvius* is a short narrow canal which connects the cavity of the fourth with the cavity of the third ventricle. It is lined by the ependyma and surrounded by a layer of gray matter continuous with that forming the floor of the fourth ventricle. In that portion of the gray matter lying beneath or ventral to the aqueduct there are groups of nerve-cells which give origin to axons which unite to form the third and fourth cranial nerves.

THE CORPORA QUADRIGEMINA

The **corpora quadrigemina** are four small grayish eminences situated beneath the posterior border of the corpus callosum and behind the third ventricle. They rest upon the lamina quadrigemina, which forms the roof of the aqueduct of Sylvius. The superior pair are the larger and are known as the *superior quadrigeminal bodies*, the *superior colliculi* or the *pregemina;* the inferior pair are the smaller and are known as the *inferior quadrigeminal bodies*, the *inferior colliculi*, or the *post-gemina*.

External and somewhat inferior to the corpora quadrigemina are two small collections of gray matter the more external of which has been termed the *external geniculate body* or the *pregeniculum*, the more internal of which has been termed the *internal geniculate body* or the *post-geniculum*.

Though these bodies are closely associated anatomically, they differ in origin, in their relations, and in their functions.

On either side the fibers composing the optic tract pass to and through the geniculate bodies in which some of the fibers terminate, while others pass onward to the superior and inferior quadrigeminal bodies and there terminate. The bands of white matter associating the superior or external and the inferior or internal geniculate bodies, with the corresponding quadrigeminal bodies are known as the superior and inferior brachia respectively. The internal geniculate body gives origin to and receives fibers from the mesial portion of the optic tract which is in reality not a portion of the optic tract proper, but a commisural band (Gudden) which associates the body from which it arises with that of the opposite side. The point of decussation is in the posterior part of the optic chiasm.

The external geniculate body is a terminal station for a portion of the fine visual fibers coming from the retina. From the cells of this body new axons arise which course forward and upward, enter the internal capsule and pass by way of the optic radiation to the cortex of the occipital region of the cerebrum.

The corpora quadrigemina show on microscopic examination that they are composed of nerve-cells and nerve-fibers, both of which are so intricately arranged that it is difficult to trace their relation one to another and to adjoining structures. Some of the cells of the superior quadrigeminal body give origin to axons which pass downward and forward and terminate in brush-like expansions around the nuclei of origin of the oculo-motor, trochlear, and abducent nuclei; other cells are surrounded by the terminal branches of some of the fibers of the optic tract, though it is not probable that they are true visual fibers. Still other cells receive the terminal branches of axons the cells of origin of which are located in the occipital cortex of the cerebrum and which reach the superior quadrigeminal body by way of the optic radiation and internal capsule.

The cells of the post-geminum give origin to axons which pass upward, forward, and outward, enter the internal capsule, and pass by way of the auditory tract to the cortex of the temporo-sphenoidal region of the cerebrum. Many of the fibers of the lateral fillet, a portion of the auditory tract, terminate in brush-like expansions around these same cells. There is thus established a connected pathway between the cochlea and the temporo-sphenoidal cortex. The cells of the temporal cortex, however, send axons in the reverse direction by way of the auditory tract to the cells of the post-geminum. There is thus established a double communication between the occipital and temporal region of the cerebral cortex, and the pre-geminal and post-geminal bodies respectively.

THE BASAL GANGLIA: THE CORPORA STRIATA AND OPTIC THALAMI

The basal ganglia are collections of ganglionic matter, situated at the base of the cerebrum along the course of the nerve-fibers that pass to and from its cortical expansion. Among these ganglia the more important are the *corpora striata* and the *optic thalami*. They are made visible upon removal of the cerebrum. The general relations of these ganglia are shown in Fig. 239.

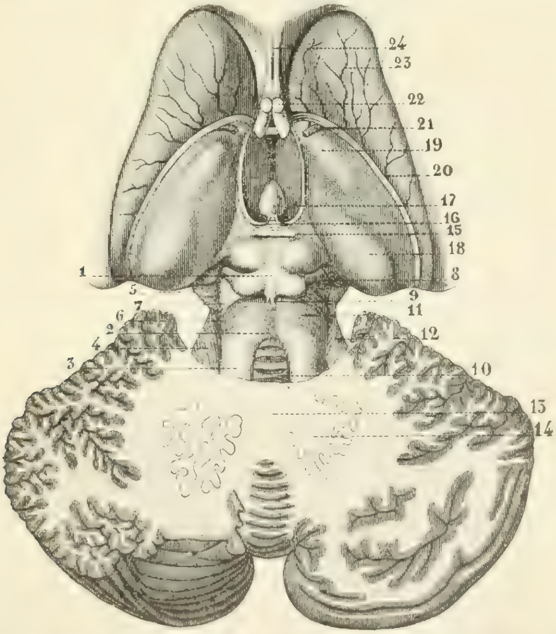

FIG. 239.—CORPORA STRIATA, OPTIC THALAMI, CORPORA QUADRIGEMINA, CEREBELLUM AND ASSOCIATED STRUCTURES. 1, Corpora quadrigemina; 2, valve of Vieussens; 3, pre-peduncle; 4, upper part of medi-peduncle; 5, upper part of crus; 6, lateral fillet; 7, band of Reil; 8 post-brachium; 9, frenulum; 10, gray matter of valve of Vieussens; 11, medi-commissure; 12, pre-commissure; 13, 14, center of cerebellum; 15, post-commissure; 16, peduncles of the pineal gland; 17, pineal gland; 18, 19, posterior and anterior tubercles of the thalamus; 20, tenia semicircularis; 21, vessels of the corpus striatum; 22, fornicolumn; 23, corpus striatum; 24, septum lucidum.—(*Sappey.*)

The **corpus striatum**, the more anterior of the two, is an ovoid collection of gray and white matter and receives its name from the fact that it presents on cross-section a striated appearance. The larger portion of this body is embedded in the cerebral white matter, while the smaller portion projects into the anterior part of the lateral ventricle. A dissection of this nucleus shows that it is subdivided by a band of white matter into two smaller nuclei, viz.: the *caudate* and the *lenticular* nuclei.

1. The *caudate nucleus* is a pyriform body which corresponds with the intra-ventricular portion of the corpus striatum. It consists of a head, an arching body and a tail. The head, which is thick and large, projects into the anterior cornu of the ventricle; the body arches across the ventricle from before backward and from within outward, while the tail is directed downward and forward to become associated with the collection of gray matter situated beneath the lenticular nucleus and known as the *amygdaline* nucleus. Anteriorly, the caudate nucleus is united with the lenticular nucleus by a narrow bridge of gray matter, partially subdivided by small bands or strands of nerve-fibers passing through it.

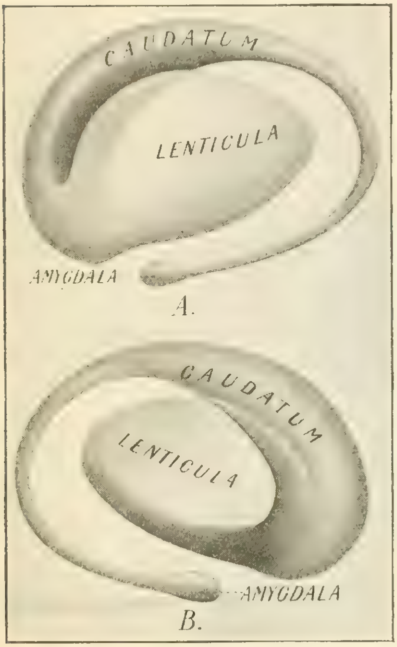

FIG. 240.—TWO VIEWS OF A MODEL OF THE STRIATUM. *A*, Lateral aspect; *B*, mesial aspect.—(*Spitzka.*)

2. The *lenticular nucleus* is an irregularly triangular pyramidal-shaped body and corresponds with the extra-ventricular portion of the corpus striatum, the portion embedded in the cerebral white matter. The apical extremity of the nucleus is directed toward the median line while its convex base is directed toward and runs almost parallel with the gray matter of the Island of Reil. The general appearance and relation of these nuclei, are shown in Figs. 240 and 241. A horizontal section of the lenticular nucleus shows that it is divided by two lamina of white matter into three portions. The two inner, from their pale yellow color, form the *globus pallidus*, the outer, somewhat darker in color, is termed the *putamen*. External to the lenticular nucleus is a thin stratum of gray matter, arranged more or less vertically, and placed between the outer surface of the lenticular nucleus and the cortex of the Island of Reil, and known as the *claustrum*.

The **optic thalamus** is an oblong mass of gray matter situated between the sensor, afferent pathway and the cortex of the cerebrum. The anterior and posterior extremities of each thalamus present enlargements known respectively as the anterior tubercle and the posterior tubercle or *pulvinar*. The mesial surface of the thalamus forms the lateral wall of the third ventricle and is covered by epithelium resting on a thin layer of ependyma.

A transection of the thalamus shows that it is not only covered externally but penetrated by white matter, which subdivides its contained gray cells into four more or less distinct masses termed nuclei, viz.: an *anterior*, a *lateral*, occupying the external part of the thalamus, a *ventral*, close to the entire ventral surface, and a *posterior*, situated beneath the pulvinar. Beneath and somewhat internal to each optic thalamus there is a region, the subthalamic, consisting of an intricate network of nerve-fibers and several nuclei of gray matter, *e.g.*, the red or tegmental nucleus, the subthalamic nucleus, or Luys' body, and the substantia nigra.

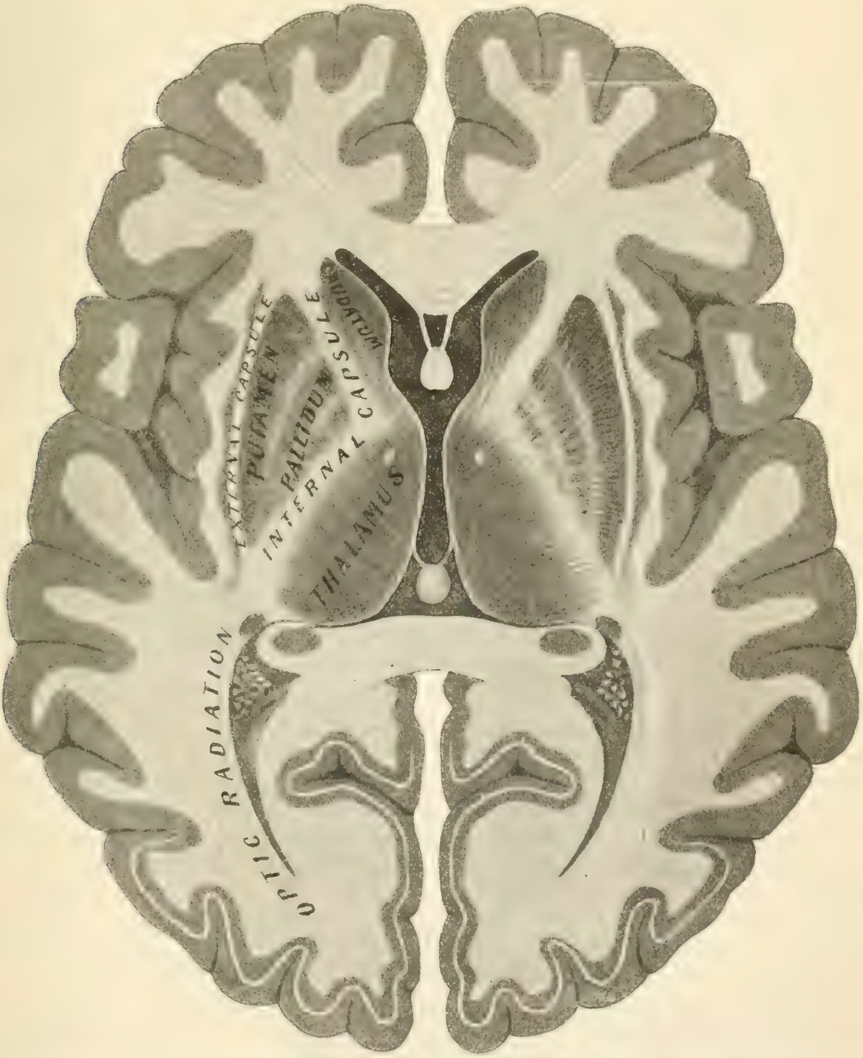
EXTERNAL CAPSULE
PUTAMEN
PALLIDUM
INTERNAL CAPSULE
CAUDATUM
THALAMUS
OPTIC RADIATION

Fig. 241.—Horizontal Section through the Cerebrum showing the Natural Relations of the Various Structures.

Though the thalamus has extensive connections with many portions of the central nerve system, the most important are with the cortex, the tegmentum, and the optic tracts.

From the cells of these various nuclei axons emerge which pass into the internal capsule, and through the corona radiata to various portions of the cortex. Those which come from the pulvinar and pass to the occipital lobe constitute a part of the optic radiation; those from the lateral and ventral nuclei ultimately reach the parietal lobe; those from the anterior nucleus pass to the hippocampal and uncinate convolutions. In a similar manner various portions of the cortex are brought into relation with the thalamus, axons from the cortical cells passing downward to terminate in tufts around the thalamic nuclei.

The tegmentum is intimately related to the thalamus, though the exact distribution of various strands of fibers is a subject of much discussion. Most of the fibers of the mesial fillet end in tufts around the cells of the ventral and lateral nuclei; other fibers pass directly to the cortex.

The optic tract sends fibers directly into the pulvinar, the external geniculate body, and the superior corpus quadrigeminum, around the cells of which they terminate in brush-like expansions.

The Internal Capsule.—The lenticular nucleus is enclosed on all sides by ascending and descending nerve-fibers. From the manner in which they surround and enclose the nucleus they have collectively been called the *lenticular capsule.* If a horizontal section of the cerebrum be made at a certain level so as to cut across the capsule and the enclosed nucleus an appearance similar to that shown in Fig. 241 will be presented. That portion of the capsule that lies between the caudate nucleus and the optic thalamus internally and the lenticular nucleus externally is known as the internal portion of the lenticular capsule or in its abbreviated form as the *internal capsule*, while that portion between the external convex border of the lenticular nucleus and the claustrum is known as the external portion of the lenticular capsule or in its abbreviated form as the *external capsule.* At a given level the internal capsule may be said to consist of two segments or limbs, an *anterior*, situated between the caudate nucleus and the anterior extremity of the lenticular nucleus, and a *posterior*, situated between the optic thalamus and the posterior extremity of the lenticular nucleus. The two segments unite at an obtuse angle, termed the knee, which is directed toward the median line. The appearance which is presented at different levels varies however considerably.

SUMMARY OF THE STRUCTURE OF THE MEDULLA, ISTHMUS, AND BASAL GANGLIA

Structure of the Central Gray Matter.—Though the general arrangement of the central gray matter has been incidentally alluded to in the foregoing presentation of the anatomic features of the medulla and isthmus, it will be convenient to summarize its arrangement and structure at this point.

The gray matter of the cord, of the dorsal aspect of the medulla and pons, of the region surrounding the aqueduct of Sylvius, and of the lining of the third ventricle, constitute practically a continuous system, though presenting modifications in various parts of its extent. In the transition region of the spinal cord and medulla the gray matter of the former becomes much changed in shape owing to the shifting of position of the various tracts of white matter, until in the medulla and pons it is spread out in the form of a thin layer near their dorsal surfaces, where, together with the ependyma, it forms the floor of the fourth ventricle.

In the region of the aqueduct of Sylvius the gray matter again converges and ultimately surrounds the canal, to again expand at its anterior extremity to form the lining of the third ventricle.

The Nerve-cells.—The nerve-cells in these different regions do not differ morphologically from those in the gray matter of the spinal cord. The corpus, or body of the cell, presents a number of dendrites as well as the sharply defined axon. As a rule, the cells are arranged in groups, or clusters, or nests, partially surrounded and enclosed by supporting tissue, and situated beneath the floor of the fourth ventricle and the floor of the aqueduct of Sylvius.

Classification of Nerve-cells.—The cells of the gray matter may be divided into three main groups; viz., intrinsic or associative, receptive or afferent and emissive or efferent.

The *intrinsic cells* are associative in function. The axons to which these cells give origin pass more or less horizontally into the white matter, where they divide into two branches, one of which passes upward, the other downward. At various levels they re-enter the gray matter and arborize around other intrinsic cells.

The *receptive cells* are largely sentient or afferent in function, inasmuch as they receive the nerve impulses transmitted to them by afferent cranial nerves. As the afferent nerve fibers are classified, in accordance with the sensations to which they give rise, as sensor, thermal, tactile, gustatory, auditory, etc., so these cells may be similarly classified, according as they transmit their excitations to those specialized areas in the cerebral cortex in which these different sensations arise.

The *emissive cells* are efferent or motor in function, inasmuch as the excitation arising in them is transmitted outwardly through their axons to muscles, glands, blood-vessels, and viscera, imparting to them motion, either molar or molecular. As the efferent fibers are classified (see page 99) in accordance with their physiologic action into motor, vaso-motor, secretor, viscero-motor, so the nerve-cells of which the nerves are integral parts may be classified physiologically as motor, vaso-motor, secretor, and viscero-motor. Collections or groups of such cells are termed "centers."

Structure of the White Matter.—The white matter is composed of medullated nerve-fibers, and though arranged in a very complex manner may be divided into longitudinal and transverse fibers.

The *longitudinal fibers* which compose the main portion of the isthmus may be subdivided into (1) a ventral or pedal portion and (2) a dorsal or tegmental portion. The fibers constituting the *ventral* or *pedal* portion may for convenience be said to extend from the cerebral cortex through the crus cerebri to the pons, medulla, and spinal cord. They may be divided into three distinct tracts: *e.g.*, the pyramidal tract, the fronto-cerebellar tract, and the occipito-temporo-cerebellar tract (Fig. 242).

The *pyramidal or motor tract* descends from the cortex of the cerebrum mainly from the gyrus anterior to the central fissure, passes through the posterior one-third of the anterior segment and the anterior two-thirds of the posterior segment of the internal capsule, the middle two-fifths of the crusta, behind the transverse fibers of the pons, to become the anterior pyramid of the medulla, beyond which it divides into the direct and crossed pyramidal tracts of the cord. In its course some of the fibers and their collaterals arborize around efferent cells from the anterior extremity of the aqueduct of Sylvius to the termination of the spinal cord.

The *fronto-cerebellar tract* descends from the cortex of the frontal gyri of the anterior lobe, passes through the anterior portion of the anterior segment of the internal capsule, the inner fifth of the crusta to the pons, where its fibers terminate or arborize around the nucleus pontis of the same and opposite sides.

The *occipito-temporo-cerebellar tract* descends from the occipital and temporal lobes, passes to the inner side of the lenticular nucleus, and continues downward on the outer side of the crusta, occupying about one-fifth of its bulk, to the pons, where its fibers also arborize around the nucleus pontis of the same and opposite sides. By means of fibers in the middle peduncle these descending fibers are brought into relation with the cerebellum. In this tract, not shown in the figure, are to be found the afferent fibers constituting the visual tract, *D* and the auditory tract *E*.

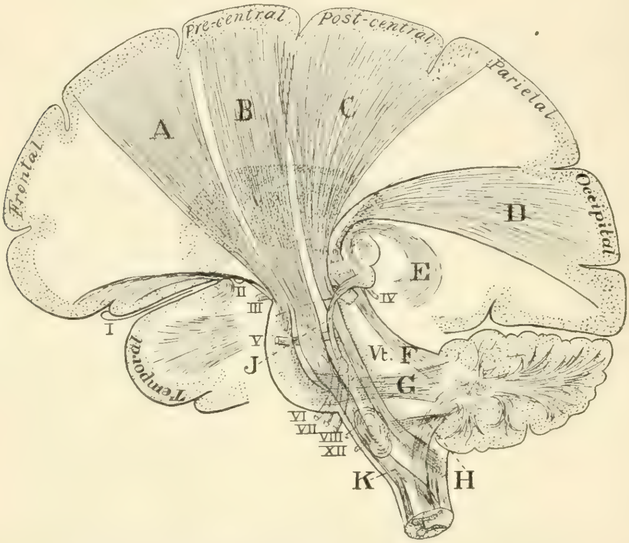

FIG. 242.—SCHEMA OF THE PROJECTION FIBERS OF THE CEREBRUM AND OF THE PEDUNCLES OF THE CEREBELLUM; LATERAL VIEW OF THE INTERNAL CAPSULE. *A*, Tract from the frontal gyri to the pons nuclei, and so to the cerebellum (frontal cerebro-cortico-pontal tract); *B*, the motor (pyramidal) tract; *C*, the sensory (body sense) tract; *D*, the visual tract; *E*, the auditory tract; *F*, the fibers of the superior peduncle of the cerebellum; *G*, fibers of the middle peduncle uniting with *A* in the pons; *H*, fibers of the inferior peduncle of the cerebellum; *J*, fibers between the auditory nucleus and the inferior quadrigeminal body; *K*, motor (pyramidal) decussation in the bulb; *Vt*, fourth ventricle. The numerals refer to the cranial nerves.—(Modified from *Starr*.)

The fibers constituting the *dorsal* or *tegmental* portion of the longitudinal system may be said for convenience to extend from the posterior portion of the medulla and pons to the optic thalamus and cerebrum. They may be subdivided into several tracts, the more important of which are the fillet and the dorsal longitudinal bundle.

The *fillet* or *lemniscus*, consisting of fibers having their origin partly from the cells of the cuneate and gracile nuclei and partly from the cells of the sensor end-nuclei of the spinal and various sensor cranial nerves, occupies a region in the ventral and mesial portion of the tegmentum throughout its entire extent. Superiorly this mesial fillet terminates for the most part around nerve cells in the nuclei of the thalamus. From these nuclei new fibers arise which pass for the most part to the cortex of the post-central and parietal gyri. The fibers coming from the sensor end-nucleus of the auditory nerve (the lateral fillet) lie on the lateral aspect of the pons and crus. Superiorly they terminate in the post-geminum (the inferior quadrigeminal body) and in the internal geniculate body. From these nuclei the fibers composing the auditory tract pass to the super-temporal convolution.

The *dorsal longitudinal bundle*, an upward extension of the fibers composing a portion of the ground bundle of the spinal cord, is located on either side of the median line just beneath the floor of the fourth ventricle and the aqueduct of Sylvius. As it passes upward collateral branches are given off, some of which arborize around the cell nuclei of the third, fourth, and sixth cranial nerves of the same side, while others cross the median line and arborize around the corresponding cell nuclei of the opposite side. Superiorly some of the fibers become related to cells in the thalamus and subthalamic region. This bundle of fibers appears to be mainly commissural in character.

The *transverse fibers* of the isthmus are found in the pons. The fibers of the ventral as well as those of the more dorsal regions have their origin in nerve-cells in the cortex of the cerebellum. From their origin they pass through the cerebellar white matter, and through the middle peduncle as far as the median line, where they decussate with fibers coming from the opposite side. Beyond this point they pass to the cerebellar cortex. From their anatomic relations it is probable that these transverse fibers are commissural in character, bringing into relation opposite but corresponding regions of the cerebellar cortex. In addition to the commissural fibers other transverse fibers associate the cerebellar cortex with the gray matter in the pons on both the same and opposite sides. In this way the cerebellum is brought into relation with longitudinal fibers coming from and going to the cerebrum.

FUNCTIONS OF THE MEDULLA OBLONGATA, ISTHMUS, CORPORA QUADRIGEMINA, AND BASAL GANGLIA

Microscopic examination of the white and gray matter of these various parts of the central nerve system shows that they are composed of nerve-cells and nerve-fibers which morphologically do not differ in essential respects from those found in the spinal cord, though their arrangement is far more complicated and involved. The functions of these closely related structures are in consequence equally complex and involved and but imperfectly known.

In a general way it may be said that by virtue of the presence of nerve-cells and definite tracts of nerve-fibers these structures collectively may be regarded as consisting:

1. Of nerve centers each of which has a special function, and
2. Of conducting paths by which these centers are brought into relation

not only with one another but with the cerebrum, the cerebellum and the spinal cord.

A. **The Medulla and Isthmus, as Local Nerve-centers.**—The emissive or efferent cells situated in the gray matter beneath the floor of the fourth ventricle and beneath the aqueduct of Sylvius and arranged in more or less well-defined groups, are the sources of the nerve energy that excites activity in the skeletal muscles, glands, vascular and to some extent visceral muscles of the head, neck, thorax and abdomen.

The efferent fibers emerging from these cells constitute in part, the trunks of the efferent encephalic or cranial nerves, the origin, course, distribution and functions of which will be considered in a subsequent chapter.

The discharge of their energy may be caused:

1. By variations in the composition of the blood or lymph by which they are surrounded or as the outcome of a reaction between the chemic constituents of the lymph on the one hand and the chemic constituents of the nerve-cell on the other hand. The excitation of the cell thus occasioned is termed *automatic* or *autochthonic* excitation.
2. By the arrival of nerve impulses, coming through afferent cranial and spinal nerves from the general periphery, skin, mucous membrane, etc.
3. By the arrival of nerve impulses descending from cells in the cortex of the cerebrum or subordinate regions.

The excitation in the former instance is said to be *reflex* or *peripheral* in origin; in the latter instance *direct* or *cerebral* in origin. In the direct or cerebral excitations the skeletal muscle movements are due to psychic states of a volitional or an affective or emotional character; the gland discharges and vascular and visceral muscle movements to emotional phases of cerebral activity only.

The activities of these centers are thus called forth by autochthonic, reflex or peripheral, and direct or cerebral excitations. The forms of activity excited in peripheral organs resemble those excited by the spinal nerve-centers. See page 451.

Special Nerve-centers.—Since it is by means of nerve-cells and their associated fibers that many important functions of organic life are initiated and maintained, it would naturally be expected from its extensive nerve connections that this region of the nerve system plays an extensive rôle in this respect. As the accomplishment of these functions requires the coöperation and coördination of a number of separate but related structures, it is evident that there must exist in the medulla and pons a number of coördinating mechanisms consisting of nerve-cells and nerve-fibers which are associated in various ways for the accomplishment of definite functions. To such a coördinating mechanism the term "center" has been given: *e.g.*, respiratory, cardiac, deglutitory, etc.[1]

Experimentation has shown that the medulla and pons contain a number of such centers, the more important of which are as follows:

1. The *cardiac centers*, which exert (1) an *accelerator* action over the heart's pulsations through nerve-fibers emerging from the spinal cord in the

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[1] By the term center as here employed is meant a collection of nerve-cells and nerve-fibers occupying an area of greater or less extent, though its exact anatomic limits may not be accurately defined. That an area may merit the term center, it is necessary that its stimulation should increase, its destruction should abolish or impair, functional activity.

roots of the first and second dorsal nerves and reaching the heart through the sympathetic nerve; (2) an *inhibitor* or *retarding* action on the rate of the heart-beat through efferent fibers in the trunk of the pneumogastric or vagus nerve. (See pages 322 and 323.)

2. A *vaso-motor center*, which regulates the caliber of the blood-vessels throughout the body in accordance with the needs of the organs and tissues for blood, through nerve-fibers passing by way of the spinal nerves to the walls of the blood-vessels. (See page 382.)
3. A *respiratory center*, which coördinates the muscles concerned in the production of the respiratory movements. (See page 425.)
4. A *mastication center*, which excites to activity and coördinates the muscles of mastication. (See page 144.)
5. A *deglutition center*, which excites and coördinates the muscles concerned in the transference of the food from the mouth to the stomach. (See page 164.)
6. An *articulation center*, which coördinates the muscles necessary to the production of articulate speech.
7. A *diabetic center* stimulation of which gives rise to glycosuria.
8. A *salivary center*, stimulation of which excites the discharge of saliva.

B. **The Medulla and Isthmus as Conductors.**—The anterior pyramids of the medulla and their continuations through the more ventral portions of the pons, being portions of the general pyramidal tract, serve to conduct volitional efferent nerve impulses from higher portions of the brain to the spinal cord. Division of these pathways is at once followed by a loss of volitional control of the muscles below the section.

The dorsal or tegmental portion, containing the fillet, serves to transmit afferent nerve impulses from the spinal cord to higher portions of the brain. Transverse division of one-half of the dorsal portion of the pons is followed by complete anesthesia of the opposite half of the body without any impairment of motion.

The restiform bodies constitute a pathway between the spinal cord and the cerebellum. The transverse fibers of the pons associate opposite but corresponding portions of the cerebellar hemispheres.

The crura cerebri consists *ventrally* of fibers which are largely derived from the pyramidal tracts and are continuous with the longitudinal fibers of the ventral portion of the pons and medulla; and *dorsally* of fibers continuous with those coming through the lower portions of the tegmentum. Hence they are conductors of motor impulses in the former and of sensor impulses in the latter region. It is not definitely known as to whether reflex actions take place through the gray matter, the locus niger, or not.

The Corpora Quadrigemina.—From the anatomic relation of the superior quadrigeminal body (the pre-geminum) to the optic tract, the inference can be drawn that it is in some way essential to the performance of various reflex ocular movements and perhaps to the variations in size of the pupil. Experimental investigations and pathologic changes support the inference.

Irritation of the pre-geminum in monkeys on one side is followed by diminution of the pupils first on the opposite side and then almost immediately on the same side. The eyes at the same time are also widely opened and the eyeballs turned upward and to the opposite side. If the irritation be continued, motor reactions are exhibited in various parts of the body. Destruction of the pre-geminum in both monkeys and rabbits is followed by blindness, dilatation and immobility of the pupils, with marked disturbance of equilibrium and locomotion (Ferrier).

From the anatomic relation of the inferior quadrigeminal body (the post-geminum) to the lateral fillet, the basal tract for hearing, the inference may be drawn that it is in some way connected with the auditory process.

Stimulation of the post-geminum gives rise to cries and various forms of vocalization. Pathologic states of this body are also attended by impairment of hearing and disorders of the equilibrium.

From the foregoing facts it is probable that the corpora quadrigemina are associated with station and locomotion. Ferrier assumes that in these bodies "sensory impressions, retinal and others, are coördinated with adaptive motor reactions such as are involved in equilibration and locomotion."

The Corpora Striata.—The relation of these bodies to the pyramidal motor tract would indicate that they are in some way connected with motor activities. Their function, however, is obscure. While stimulation of one corpus produces convulsion of the muscles of the opposite side of the body, and destruction gives rise to paralysis of the corresponding muscles, it is difficult, owing to the intimate association of the white and the gray matter, to state to which the phenomena are to be attributed. The evidence at hand points to the conclusion that if a lesion is limited to the gray matter the paralysis which might result would be but temporary and of short duration. The pathologic evidence is of a similar character. Gowers is of the opinion, that if the lesion is small and at a sufficient distance from the white fibers of the capsule, there may even be no initial hemiplegia; neither motor nor sensory paralysis will arise if the lesion is confined to the gray matter.

It is stated by some experimenters that localized injuries, both experimental and pathologic, are followed by a persistent rise of temperature, varying from 1° to 2.6°C.

The Optic Thalami.—From the anatomic relation of the optic thalami to the general and special sense nerve-tracts, on the one hand, and to the cerebral cortex, on the other hand, it is assumed that they are connected with the production of sensations both general and special, and act as intermediaries between the peripheral sense-organs and the cortex.

The results of experimental stimulation and destruction of the thalami are extremely contradictory and fail to throw much light on their functions. Ferrier states that destruction of the posterior part of one thalamus produced blindness in the opposite eye and impairment of the sense of touch and pain in the opposite side of the body. In a patient under the care of Hughlings Jackson there was blindness in the right half of each eye, loss of hearing in the left ear, impairment of taste on the left side of the tongue, and a diminution of the sense of touch on the left side of the body. Post-mortem examination showed a patch of softening in the posterior part of the right thalamus, the remainder of the organ being normal.

It is probable that in the thalamus visual, tactile, and labyrinthine impressions are received, coördinated, and reflected outward, with the result of producing various adaptive motor reactions connected with station and equilibrium. The thalamus is believed by some investigators to act also as an intermediary between emotional states and their expression in the muscles of the face, this power being lost in certain pathologic conditions. The power of regulating the temperature of the body has been also assigned to the thalamus, as destruction of its anterior extremity is usually followed by a rise in temperature.

The Internal Capsule.—The internal capsule has been shown by the results both of experiment and of pathologic processes to be, first, a pathway for the transmission of nerve impulses from the cerebral cortex to the pons, medulla, and spinal cord, which give rise to contraction of the muscles of the opposite side of the body; and, second, a pathway for the transmission of nerve impulses coming from skin, mucous membrane, muscles, and special sense-organs to the cortex, where they give rise to sensations general and special. It is therefore the common motor and sensor pathway. For the reason that it transmits both motor and sensor impulses, and for the further reason that it is frequently the seat of pathologic lesions which are followed by either a loss of motion or sensation or both, the internal capsule is one of the most interesting parts of the central nerve system. As shown in Fig. 243, it consists of two segments or limbs united at an obtuse angle, the knee or elbow, which is directed toward the median line. The *motor* tract is confined to the posterior one-third of the anterior segment and the anterior two-thirds of the posterior segment. The *sensor* tract is confined to the posterior one-third of the posterior segment, the extreme end of which also contains the optic and auditory tracts.

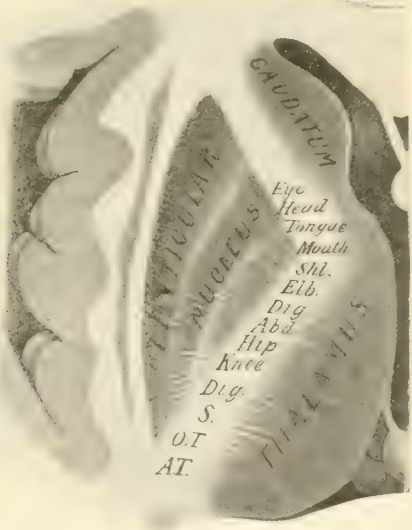

Fig. 243.—Horizontal Section of the Internal Capsule Showing the Position and Relation of the Motor Tracts for the Eye, Head, Tongue, Mouth, Shoulder (Shl.), Elbow (Elb.), Digits of Hand (Dig.), Abdomen (Abd.), Hip, Knee (Kn.), Digits of Foot (Dig.). S. Sensor tract. O. T. Optic tract. A. T. Auditory tract.

The region of the anterior segment in front of the motor tract contains the fibers of the fronto-cerebellar tract, the function of which is unknown.

The motor region contains fibers which descend from the cerebral cortex to nerve-centers situated in the gray matter beneath the aqueduct of Sylvius, in the gray matter beneath the floor of the fourth ventricle, and in the anterior horns of the gray matter of the spinal cord, and which in turn are connected by the cranial and spinal nerves with the muscles of the eye, head, face, trunk, and limbs. The positions occupied by these different tracts are shown in Fig. 243. The relation of the internal capsule to the caudate nucleus and the optic thalamus internally, and to the lenticular nucleus externally, is also shown in a vertical section of the cerebrum made in front of the gray commissure (Fig. 244).

From the fact that the internal capsule contains efferent or motor tracts, and afferent or sensor tracts, it is evident that a destructive lesion of the motor tract would be followed by a loss of motion; and of the sensor tract, by a loss of sensation on the opposite side of the body.

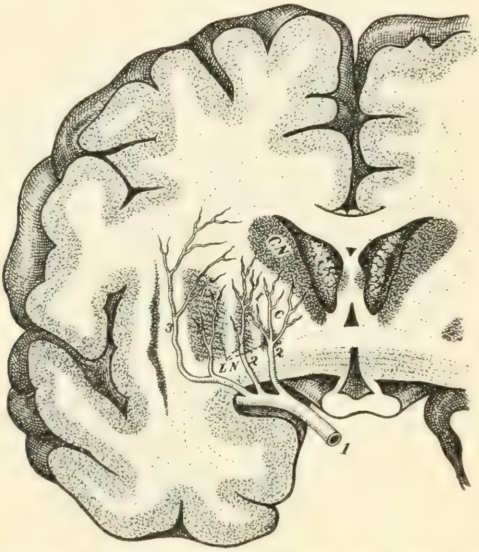

FIG. 244.—A TRANSVERSE SECTION OF ONE-HALF OF THE CEREBRUM. Arteries supplying the lenticular nucleus *LN*, the internal capsule *IC*, and the caudate nucleus *CN*. 1. The middle cerebral. 2, 2. Lenticular arteries. 3. The lenticulo-striate artery passing through the external capsule.

This condition, to a greater or less extent, frequently arises in consequence of a rupture of the blood-vessels which supply the caudate nucleus, the lenticular nucleus and the internal capsule. These arteries, branches of the middle cerebral, penetrate the brain in the anterior and posterior perforated spaces (Fig. 244). By reason of a diseased condition of their walls, especially of the lenticulo-striate artery, the vessel ruptures and the blood is extravasated into the surrounding tissues.

If the extravasation occurs in the anterior two-thirds of the posterior limb of the internal capsule, there will be a destruction of the efferent or motor fibers, and a separation of the cortical motor area from the medullary and spinal motor nuclei and, therefore, a loss of volitional control of the muscles of the face, arm and leg of the opposite side. The extent of this paralysis will depend, of course, on the extent of the extravasation. The muscles of the larynx, thorax and abdomen, those associated with symmetrical movements escape paralysis for the reason that in all such movements each side of the brain controls the muscles of both sides of the body. If the extravasation of blood also destroys the fibers of the posterior, one-third of the internal capsule in the region between the optic thalamus and the lenticular nucleus, there will be a destruction of the afferent or sensor fibers and a separation of the cutaneous areas from the cortical sensor areas and, therefore, a loss of sensation on the opposite side of the body. If the extravasation is confined to the external limits of the posterior one-third of the capsule, there would be a loss of sensation without impairment of motion, a rare condition however. In these hemorrhages the optic and auditory tracts are seldom involved. Coincident with the rupture of these vessels there is a loss of consciousness as a rule, and the patient falls as if struck and hence this condition received the name of apoplexy. With the recovery of consciousness the paralysis of motion becomes apparent and is usually permanent. Not infrequently, however, partial recovery of motion and sensation takes place after the blood coagulates and the serum is absorbed, thus relieving pressure on adjoining nerve-tracts which were not otherwise injured.

CHAPTER XXIII

THE CEREBRUM

The **cerebrum** is the largest portion of the encephalon, constituting about 85 per cent. of its total weight. In shape it is ovate, convex on its outer surface, narrow in front and broad behind. It is divided by a deep longitudinal cleft or fissure into halves, known as the cerebral hemispheres. The hemispheres are completely separated anteriorly and posteriorly by this fissure, but in their middle portions are united by a broad white band of nerve-fibers, the corpus callosum. Each hemisphere or hemi-cerebrum is convex on its outer aspect, and corresponds in a general way with each side of the cavity of the skull; the inner or mesial surface is flat and forms the lateral boundary of the longitudinal fissure.

The surface of each hemi-cerebrum presents a series of alternate indentations and elevations, known respectively as fissures or sulci, and convolutions or gyri. A knowledge of the situation and extent of the principal fissures and convolutions, as well as of their relation one to another, is essential to a clear understanding of many physiologic processes, clinical phenomena, and surgical procedures. The general arrangement of the primary fissures and convolutions is represented in Figs. 245 and 246.

Fissures.—

1. The *Sylvian fissure*, one of the most important of the primary fissures, is found on the side of the cerebrum. It begins at the base and extends upward, outward, and backward to a point corresponding to the eminence of the parietal bone, where it usually terminates in a more or less vertically directed branch, the epi-sylvian branch. Anteriorly a short branch is given off which passes upward and forward into the frontal lobe and known as the pre-sylvian; a horizontal branch is known as the sub-sylvian. The Sylvian fissure is the first to appear in the development of the fetal brain, becoming visible at the third month. In the adult it is deep and well marked and divides the hemi-cerebrum into a frontal and a temporo-sphenoidal lobe.
2. The *Rolandic* or *central fissure*, equally important, is found on the superior and lateral aspects of the cerebrum. It runs from a point on the convexity of the hemisphere near the median line transversely outward and downward toward the fissure of Sylvius, but as a rule does not pass into it. It divides the frontal from the parietal lobe. The inclination of the central fissure is such as to form with the longitudinal fissure an angle of about 70 degrees.
3. The *intra-parietal fissure* arises a short distance behind the central fissure. It then runs upward, backward, and downward to terminate near the posterior extremity of the parietal lobe. It divides the parietal lobe into a superior and an inferior portion.

4. The *parieto-occipital fissure,* situated on the mesial surface of the hemispheres, divides the latter into a parietal and an occipital lobe. It begins as a deep notch on the surface of the hemisphere, and is then continued downward and forward until it enters the calcarine fissure. (Fig. 246.)

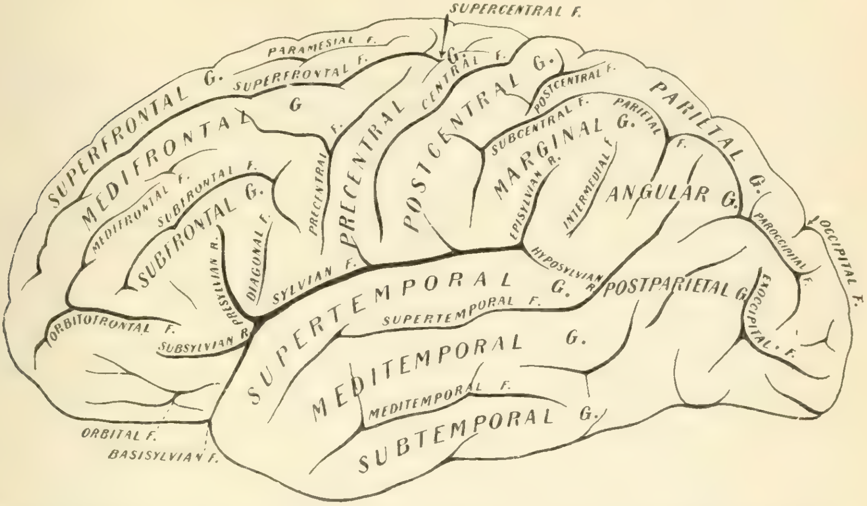
SUPERCENTRAL F.
PARAMESIAL F.
G.
CENTRAL F.
SUPERFRONTAL G.
SUPERFRONTAL F.
G
MEDIFRONTAL
PRECENTRAL
F.
POSTCENTRAL G.
POSTCENTRAL F.
PARIETAL G.
SUBCENTRAL F.
PARIETAL
F.
MARGINAL G.
MEDIFRONTAL F.
SUBFRONTAL F.
SUBFRONTAL G.
PRECENTRAL
POSTCENTRAL
EPISYLVIAN R.
INTERMEDIAL F.
ANGULAR G.
PAROCCIPITAL F.
OCCIPITAL F.
PRESYLVIAN R.
DIAGONAL F.
SYLVIAN F.
HYPOSYLVIAN R.
SUPERTEMPORAL G.
POSTPARIETAL G.
EXOCCIPITAL F.
ORBITOFRONTAL F.
SUBSYLVIAN R.
SUPERTEMPORAL F.
MEDITEMPORAL G.
MEDITEMPORAL F.
SUBTEMPORAL G.
ORBITAL F.
BASISYLVIAN F.

FIG. 245.—FISSURES AND GYRI ON THE LATERAL SURFACE OF THE LEFT HEMI-CEREBRUM.— F. Fissure. G. Gyrus. R. Ramus.—(*Spitzka.*)

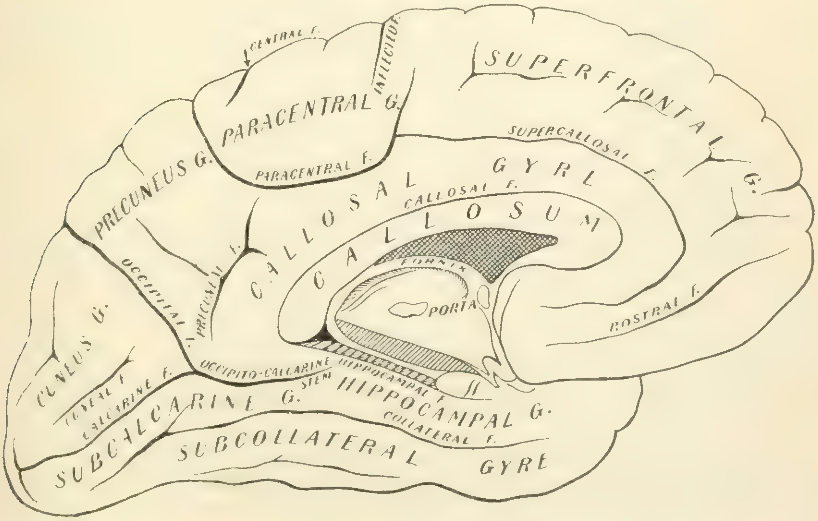
CENTRAL F.
INFLECTED F.
PARACENTRAL G.
SUPERFRONTAL G.
SUPERCALLOSAL F.
PRECUNEUS G.
PARACENTRAL F.
CALLOSAL GYRE
CALLOSAL F.
CALLOSUM
FORNIX
OCCIPITAL F.
PRECUNEAL F.
PORTA
ROSTRAL F.
CUNEUS G.
OCCIPITO-CALCARINE
STEM
HIPPOCAMPAL F.
CUNEAL F.
CALCARINE F.
SUBCALCARINE G.
HIPPOCAMPAL G.
COLLATERAL F.
SUBCOLLATERAL GYRE

FIG. 246.—FISSURES AND GYRI OF THE MESIAL SURFACE OF THE LEFT HEMI-CEREBRUM. —(*Spitzka.*)

5. The *calcarine fissure* begins on the posterior extremity of the mesial surface of the occipital lobe. From this point it passes downward and forward to unite with the parieto-occipital fissure.

6. The *para-central fissure* begins at the supero-mesial border of the hemisphere. It then passes downward and forward for a variable distance and then turns upward enveloping a lobule known as the *para-central* lobule.
7. The *super-callosal fissure* extends from a point just anterior to the para-central lobule downward and forward below the rostrum of the corpus callosum.

Secondary fissures of more or less importance are present in the different lobes, subdividing the surface into convolutions: *e.g.*, in the frontal lobe are found the *pre-central*, the *super-frontal*, *medi-frontal and sub-frontal fissures;* in the temporal lobe the *super-temporal* and *medi-temporal fissures*.

Convolutions.—The convolutions or gyri are the portions of the cerebral surface comprised between the fissures. The arrangement of the surface is such that only the more superficial portions are visible. The depth of the convolution, the portion bordering the fissure, is concealed from view. Each lobe presents a series of such convolutions which differ considerably in their relative physiologic importance.

The Frontal Lobe.—The frontal lobe presents on its convex surface four convolutions, viz.: the anterior or pre-central convolution, and the super-, medi-, and sub-frontal convolutions.

1. The *anterior or pre-central convolution* or *gyrus* is situated just in front of the Rolandic or central fissure, with which it corresponds in direction. It is continuous above with the super-frontal and below with the sub-frontal convolution.
2. The *super-frontal convolution* or *gyrus* is bounded internally by the longitudinal fissure and externally by the super-frontal fissure. From the upper end of the pre-central convolution, with which it is continuous, it runs forward and downward to the anterior extremity of the frontal lobe, where it turns backward and rests on the orbital plate of the frontal bone.
3. The *medi-frontal convolution* or *gyrus* is situated on the side of the lobe, between the super-frontal fissure above and the medi-frontal fissure below. Its general direction is downward and forward.
4. The *sub-frontal convolution* or *gyrus* winds around the pre-sylvian branch of the fissure of Sylvius in the anterior and inferior portion of the frontal lobe. It is continuous posteriorly with the lower end of the pre-central convolution.

The Parietal Lobe.—The parietal lobe presents three well-marked convolutions, viz.: the posterior or post-central convolution, and the super- and sub-parietal. The latter is again subdivided into the marginal and the angular convolution.

1. The *posterior or post-central convolution* or *gyrus* is situated just behind the Rolandic or central fissure, with which it corresponds in direction. Above, it is continuous with the super-parietal convolution; below, with the marginal and the pre-central convolutions.
2. The *super-parietal convolution* or *gyrus* is bounded internally by the longitudinal fissure and externally by the intra-parietal fissure. From the upper end of the post-central convolution, with which it is connected, it runs downward and backward as far as the parieto-occipital fissure.
3. The *sub-parietal convolution* or *gyrus* is connected anteriorly with the

post-central convolution. Passing backward, it winds around the superior extremity of the fissure of Sylvius, in which situation it is known as the *supra-marginal* convolution. Beyond this point it divides into two portions, one of which runs forward into the temporal lobe above the super-temporal fissure, while the other runs downward and backward, following the intra-parietal fissure to its termination. At this point it makes a sharp bend and runs forward into the temporal lobe just beneath the super-temporal fissure. In the neighborhood of the bend it is generally known as the *angular convolution* or *gyrus.*

The Temporo-sphenoidal Lobe.—The temporo-sphenoidal lobe presents on its external surface three well-marked convolutions: viz., the *super-*, the *medi-*, and the *sub-temporal*, separated by the super- and medi-temporal fissures. These three convolutions are in a general way parallel with each other, and pursue a direction from before backward and upward. Anteriorly, they are fused together, but posteriorly their connections are somewhat different. The super-temporal is continuous behind and above with the *supra-marginal* convolution, and behind and below with the *angular* convolution or gyrus. The medi-temporal blends with the preceding and with the middle occipital. The sub-temporal is continuous with the inferior occipital.

The Occipital Lobe.—The occipital lobe is triangular in shape and forms the posterior apex of the hemisphere. Its base on the external surface is formed by an imaginary line drawn from the parieto-occipital fissure to the pre-occipital notch on the inferior and lateral border. The external surface presents three convolutions—the superior, middle, and inferior occipital.

The **inner** or **mesial surface** of the hemisphere, formed in part by the frontal, the parietal, the occipital, and the temporal lobes, presents several convolutions of much physiologic interest, viz.:

1. The *callosal convolution*, or *gyrus*, situated between the super-callosal fissure and the corpus callosum. From its origin anteriorly at the base of the brain this convolution passes backward, gradually increasing in width as it approaches the posterior extremity of the corpus callosum. At this point it again narrows and descends between the calcarine and hippocampal fissures to blend with the hippocampal convolution.
2. The *hippocampal gyrus*, formed by the union of the posterior extremity of the callosal convolution and the sub-calcarine convolution is situated just below the dentate or hippocampal fissure. Anteriorly it becomes enlarged, and just behind the apex of the temporal lobe turns backward and inward to form a hook-shaped eminence, the *uncinate gyrus* or *uncus.*

   The *limbic lobe* is the name given to an area of the brain which includes, among other structures, the callosal convolution, the gyrus hippocampus, and the uncus. As forming a part of this general lobe may be mentioned the dentate fascia, the striæ and peduncle of the corpus callosum, the septum lucidum, the fornix, and the infra-callosal gyrus.
3. The *sub-collateral convolution or gyrus* is bounded by the collateral fissure above, and its inferior border extends from the occipital lobe to the anterior pole of the temporal lobe.

4. The *quadrate lobule, or precuneus*, a square-shaped convolution, is situated between the posterior termination of the para-central fissure and the parieto-occipital fissure. It blends with the callosal convolution, on the one hand, and with the parietal lobule on the other.
5. The *cuneus*, a triangular or wedge-shaped convolution or lobule, is situated on the mesial surface of the occipital lobe between the parieto-occipital and calcarine fissures.

The Insula or Island of Reil.—This anatomic structure consists of a triangular-shaped cluster of six small convolutions situated at the bifurcation of the Sylvian fissure and concealed from view by the convolutions bordering it, spoken of collectively as the operculum. These convolutions are connected with the frontal, the parietal, and the temporal lobes.

Structure of the Gray Matter of the Cortex.—The gray matter, the cortex of the cerebrum, varies from two to four millimeters in thickness. When examined with a lens of low power, it presents a laminated appearance, due to differences in color and arrangement of its constituent elements. With higher magnification the cortex is seen to consist of neuroglia cells, nerve-cells with specialized dendrites and axons, medullated and non-medullated nerve-fibers, blood-vessels, connective tissue, etc., all of which are arranged and interblended in a most intricate manner. Notwithstanding the complexity of its structure, modern histologic methods have enabled Cajal to divide it into four fairly distinct layers or zones, from without inward, as follows (Fig. 247):

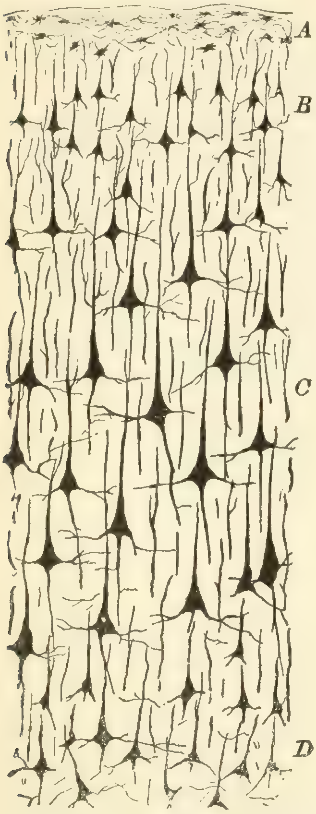

FIG. 247.—SECTION OF THE CEREBRAL CORTEX (MOTOR AREA) OF CHILD, STAINED BY GOLGI'S SILVER METHOD. *A*. Layer of neuroglia cells. *B*. Layer of small pyramidal ganglion cells. *C*. Layer of large pyramidal cells. *D*. Layer of irregular smaller cells.—(*Piersol.*)

1. *The Molecular Layer.*—The most superficial portion of this layer consists mainly of neuroglia or glia cells, the processes of which interlace in all directions, forming a distinct sheath just beneath the pia. The deeper portions of this layer contain a specialized type of nerve-cells (Cajal cells), of which there are several varieties. These cells give off nerve-fibers which pursue a horizontal direction for a variable distance, but in their course give off collateral branches which ascend to the outer surface of the layer. Among these structures are to be found, also, dendritic processes of cells situated in the subjacent layer. The terminal filaments of medullated nerve-fibers coming from nerve-cells in lower regions of the encephalo-spinal axis are also present, but for the most part they pursue a tangential direction.

2. *The Layer of Small Pyramidal Cells.*—This layer consists mainly of nerve-cells, the majority of which are pyramidal in shape and of small size. Other cells, however, are present, which present a variety of shapes, for which reason the layer was at one time termed the ambiguous layer. The apical process of the pyramidal cells is broad at the base, but narrows rapidly as it passes upward. It frequently divides into several branches, each of which develops club-shaped processes or gemmules, which give to it a feathery appearance. Dendrites are also given off from the sides and base of the cell-body. From the base a single axon descends, which ultimately becomes the axis-cylinder of a medulated nerve.
3. *The Layer of Large Pyramidal Cells.*—The nerve-cells of this layer, as the name implies, are also pyramidal in shape, but of large size. Each cell presents the same features as the cells of the preceding layer, with the exception that the apical process is larger, better developed, and branches more freely. All the dendrites are extensively provided with gemmules. The axon is well developed, sharply defined, and smooth. After giving off collateral branches, the axon descends into the cerebrum and becomes a medullated nerve-fiber.
4. *The Layer of Polymorphous Cells.*—In this layer the nerve-cells present a variety of forms: *e.g.*, spindle, polygonal, pyramidal, etc. The spindle form is the most common. From either end of the spindle a large dendrite emerges, soon branches, and becomes gemmulated. The axon is well defined and it soon descends into the white matter.

The Number of Cortical Cells.—Attempts have been made by various histologists to estimate the total number of functional nerve-cells in the cerebral cortex of man. Though the estimates are widely different, the lowest presents numbers which are beyond comprehension. Thus, Meynert's estimate is 612 millions; Donaldson's estimate for the entire brain is 12,000 millions; and Thompson's 9283 millions.

Structure of the White Matter.—The white matter of the cerebrum consists of medullated nerve-fibers which, though intricately arranged, may be divided into three systems: viz., the commissural, the association, and the projection.

1. *The commissural system.*—The fibers which compose this system unite corresponding areas of the cortex of each hemisphere. The fibers from the frontal, parietal, and occipital lobes cross in the median line and form a band of transversely arranged fibers, the corpus callosum. The fibers which unite the corresponding areas of the temporo-sphenoidal lobes cross in the anterior commissure. All the commissural fibers are the axons of nerve-cells in the cortex, the terminals of which are to be found in the cortex of the opposite side.
2. *The association system.*—The fibers which compose this system unite neighboring as well as distant parts of the same hemisphere, and may therefore be divided into long and short fibers. They associate the inexcitable or association areas with the excitable or projection areas.
3. *The projection system.*—The fibers composing this system unite certain areas of the cortex of the cerebrum with the basal ganglia, the pons, medulla oblongata, and spinal cord. They may be divided into: (1) afferent fibers which have their origin in the lower nerve-centers at dif-

ferent levels and thence pass to the cortex; and (2) efferent fibers which have their origin in the cortex and thence pass to the lower nerve-centers, terminating at different levels. The former are also termed the *cortico-afferent* or *cortico-petal;* the latter, *cortico-efferent* or *cortico-fugal.*

The *afferent fibers*, the so-called sensor tract, which transmit nerve impulses coming from the general periphery and the sense-organs, pass through the tegmentum as the mesial and lateral fillets, and thence to the cortex directly by way of the internal capsule, or indirectly through the intermediation of the thalamic and subthalamic nuclei. (See Fig. 242, page 562.) The distribution of these fibers to the various areas of the cortex will be stated in subsequent paragraphs.

The *efferent fibers* of the so-called motor tract which transmit motor or volitional nerve impulses from the cortex to the pons, medulla, and spinal cord, emerge from the layer of pyramidal cells of the gray matter of the anterior or the pre-central convolution, the para-central lobule, and immediately adjacent areas. From this origin the axons descend through the white matter of the corona radiata, converging toward the internal capsule, into and through which they pass, occupying the anterior two-thirds of the posterior limb or segment. Beyond the capsule they continue to descend, occupying the middle three-fifths of the pes or crusta of the crus cerebri, the ventral portion of the pons, and eventually the anterior pyramid of the medulla oblongata. At this point the tract divides into two portions, viz.:

1. A large portion, containing from ninety-one to ninety-seven per cent. of the fibers, which decussates at the lower border of the medulla and passes down the lateral column of the cord, constituting the *crossed pyramidal tract.*
2. A small portion, containing from three to nine per cent. of the fibers, which does not decussate at the medulla, but passes down the inner side of the anterior column of the same side, constituting the *direct pyramidal tract* or column of Türck.

After passing through the internal capsule, and as it descends through the crus, pons, and medulla, the cortico-efferent tract gives off a number of fibers which cross the median line and arborize around the nerve-cells of the gray matter beneath the aqueduct of Sylvius (the nuclei of origin of the third and fourth cranial nerves), and around the nerve-cells in the gray matter beneath the floor of the fourth ventricle (the nuclei of origin of the remainder of the motor cranial nerves). The remaining fibers go to form the crossed and direct pyramidal tracts and arborize around the cells in the anterior horn of the gray matter of the opposite side of the cord at successive levels. By this means the cortex is brought into anatomic and physiologic relation with the general musculature of the body through the various cranial and spinal motor nerves. (See Fig. 234, page 549.)

The *fronto-cerebellar* and the *occipito-temporo-cerebellar* tracts are also efferent tracts and parts of the projection system. The fronto-cerebellar, originating in the nerve-cells of the cortex of the frontal lobe, passes down to and through the internal capsule, occupying the anterior one-third of the anterior segment. It then descends along the inner side of the crus cerebri to the pons, where its fibers arborize around the cells of the *nucleus pontis.* Through the intermediation of these cells this tract is brought into relation with the cerebellum of the same but chiefly of the opposite side. The occipito-temporal tract, originating in the cells of the cortex of both the occipital and temporal lobes, passes downward and inward toward the lenticular nucleus, beneath which it passes to enter the outer one-fifth of the crusta. It then enters the pons, and through the nucleus pontis also comes into relation with the cerebellum of both sides. (See Fig. 242, page 562.)

THE FUNCTIONS OF THE CEREBRUM

The functions of the cerebrum comprehend, in man at least, all that pertains to sensation, cognition, feeling, and volition. All subjective experiences, which in their totality constitute mind, are dependent on and associated with the anatomic integrity and the physiologic activity of the cerebrum and its related sense-organs, the eye, ear, nose, tongue, etc.

From an examination of the anatomic development of the brain in different classes of animals, in different men and races of men, and from a study of the pathologic lesions and the results of experimental lesions of the brain, evidence has been obtained which reveals in a striking manner the intimate connection of the cerebrum and all phases of mental activity.

1. *Comparative anatomic* investigations show that there is a general connection between the size of the brain, its texture, the depth and number of convolutions, and the exhibition of mental power. Throughout the entire animal series an increase in intelligence goes hand in hand with an increase in the development of the brain. In man there is an enormous increase in size over that of the highest animals, the anthropoid apes. The most cultivated races of men have the greatest cranial capacity, that of the educated European or American being approximately 92.1 cubic inches (1835 c.c.); while that of the Australian is but 81.7 cubic inches (1628 c.c.). Men distinguished for great mental power usually have large and well-developed brains; *e.g.*, that of Cuvier weighed 64.4 ounces (1830 grams); that of Abercrombie, 63 ounces (1786 grams). A large intelligence, however, is not incompatible with a much smaller brain weight; thus, the brain of Helmholtz weighed but 50.8 ounces (1440 grams); that of Leidy, 49.9 ounces (1415 grams); that of Liebig, 47.7 ounces (1352 grams). The average brain weight of 96 distinguished men has been found to be 51.9 ounces (1473 grams) (Spitzka).
2. *Pathologic lesions* and mechanic injuries which disorganize the cerebrum are at once followed by a disturbance or an entire suspension of mental activity. Concussion of the brain or sudden compression from a hemorrhage destroys consciousness. Physical and chemic alterations of the gray matter of the cerebrum have been shown to coexist with insanity, loss of memory, loss of articulate speech, etc. Congenital defects of organization are accompanied by a deficiency in mental capacity and the higher instincts. Under such circumstances no great advance in brain development is possible and the intelligence remains at a low level. In congenital idiocy the brain is small, imperfectly developed, and wanting in proper chemic composition.
3. *Experimental lesions* of the brain in lower animals are attended by results similar to those observed in disease or after injury in man. Removal

of the cerebrum in the pigeon completely abolishes intelligence and destroys the capability of performing volitional movements. The pigeon remains in a state of profound stupor, though retaining the capability of executing reflex or instinctive movements. It can temporarily be aroused by loud noises, light placed before the eyes, pinching of the toes, etc., but it soon relapses into a condition of quietude. Coincident with the destruction of the cerebrum there occurs a loss of memory, reason, and judgment, and the animal fails to associate the impressions with any previous train of ideas. The higher the animal in the scale of development, the more striking is the loss of mentality after removal of the cerebrum.

4. *Experimental interference* with the blood-supply to the cerebrum is followed by a diminished or complete cessation of its activities. There is perhaps no organ of the body that is so directly dependent upon its blood-supply for the continuance of its activities as the cerebrum. The supply of blood is furnished by four large blood-vessels: viz., the two carotid and the two vertebral arteries. These vessels, after entering the cavity of the skull, give off branches which unite to form the "circle of Willis." From this circle, large branches are given off which enter the cerebrum and distribute blood to all its parts. After passing through the capillaries the blood, greatly altered in chemic composition, is returned by large veins. The large volume of blood that is present in the brain and the marked changes in composition that it undergoes while passing through the brain indicate a very active and complex metabolism in this organ. By means of the anatomic arrangement of the blood-vessels at the base of the brain, the blood-supply is equalized. It also explains why, when one, or even two, of the four large vessels are occluded by pathologic deposits or surgical procedures, brain activity continues, though perhaps diminished in degree. Occlusion of all four vessels, however, is at once followed by a complete abolition of all forms of cerebral activity. An experiment performed by Brown-Séquard illustrates the dependence of cerebral activity on the blood-supply. A dog was beheaded at the junction of the neck and chest. After a period of ten minutes all evidences of life had entirely ceased. Four tubes connected with a reservoir of warm defibrinated blood were then connected with the four arteries of the head. By means of a pumping apparatus imitating the action of the heart the blood was driven into and through the brain. After a few minutes cerebral activity returned, as shown by contractions of the muscles of the face and eyes. The character of the contractions were such as to convey the idea that they were directed by the will. These vital manifestations continued for a period of fifteen minutes, when on the cessation of the artificial circulation they disappeared, and the head exhibited once more the usual phenomena observed in dying: viz., contraction and then dilatation of the pupils and convulsive movements of the muscles of the face.

The Localization of Functions in the Cerebrum.—By the term, localization of functions, is meant the assignment of definite physiologic functions to definite anatomic areas of the cerebral cortex. From experiments made on the brains of animals, by the observation and association of clinical symptoms with pathologic lesions of the central nerve system, and from observation of the developmental stages of the embryonic brain, it has been established in recent years:

1. That the general and special sense-organs of the body are associated through afferent nerve-tracts with definite though perhaps not sharply delimited areas of the cerebral cortex; and—
2. That certain areas of the cortex are associated through efferent nerve-tracts with special groups of skeletal or voluntary muscles.

Experimental excitation of a cortical area associated with a sense-organ is undoubtedly attended by the production of a sensation at least similar to that produced by peripheral excitation of the sense-organ itself; *destruction* of the area is followed by an abolition of all the sensations associated with the sense-organ. For these reasons such areas are termed *sensor.*

Experimental excitation of a cortical area associated with a group of skeletal muscles is attended by their contraction; *destruction* of the area is followed by their relaxation or paralysis. For these reasons such areas are termed *motor.*

Since the sense-organs are remote from the brain and the impressions made upon them by the objective world can be utilized in the mental life only after they have been reproduced in the cortical areas, it may be said that each sense-organ has its special area in the cortex by which it is represented, or, in other words, each sense-organ has a cortical area of representation.

Since the muscles are remote from the brain and since they contract in response to the discharge of nerve impulses from the cells of the cortical motor areas, it may be said that the mental activities associated with the motor areas are represented by the contractions of the muscles; in other words, that the cortical motor areas have areas of representation in the general skeletal musculature. It is usually stated, however, in the reverse way: viz., that the muscle movements have areas of representation in the cortex.

The cortex of the cerebrum may therefore be compared to a mosaic made up, partially at least, of sensor and motor areas which respectively represent sense-organs and motor organs, and which bear a definite anatomic and physiologic relation one to the other. Their coöperation is essential to the normal performance of many forms of cerebral activity.

A knowledge of the situation of these areas, the order of their development, the effects that arise from their stimulation or follow their destruction, are matters of the highest importance in the study of cerebral activity and indispensable to the physician in the localization of lesions which manifest themselves in perversions or abolition of sensations and in convulsive seizures or paralyses.

The Sensor Areas.—The sensor areas which should theoretically be present in the cortex are primarily those which receive and translate into conscious sensations nerve impulses, developed by changes going on in the body itself; and secondarily those which receive and translate into conscious sensations the nerve impulses developed in the special sense-organs by the impact of the external or objective world. In the former areas, are received the nerve impulses that come from the mucous membranes, muscles, joints, viscera, etc., and give rise to muscle, and visceral sensations. In the latter areas are received the nerve impulses that come from the sense-organs and give rise to cutaneous, gustatory, olfactory, auditory, and visual sensations. A number of such sense areas may be predicated: *e.g.*, areas of *cutaneous* and *muscle sensibility*, of *gustatory*, *olfactory*, *auditory*, and *visual sensibility*.

The Motor Areas.—The motor areas which should theoretically be present in the cortex are those which in consequence of the discharge of nerve impulses excite contraction of special groups of muscles and which, from their coördinate and purposive character, are conventionally termed volitional. Five such general motor areas may be predicated: *e.g.*, one for the muscles of the head and eyes, one for the muscles of the face and associated organs, and others for the muscles of the arm, leg, and trunk. They are usually designated as *head and eye*, *face*, *arm*, *leg*, and *trunk motor areas*.

The existence and anatomic location of these areas in the cortex of animals have been determined by the employment of two methods of experimentation: viz., stimulation and destruction or extirpation; the first by means of the rapidly repeated induced electric currents, the second by the electric cautery and the knife.

If the stimulation of a given area is attended by phenomena which indicate that the animal is experiencing sensation, and its destruction by a loss of this capability or the loss of a special sense, it is assumed that the area is *sensor* in function—is an *area of special sense*. If the stimulation or excitation of any given area is followed by contraction, and its destruction by paralysis of muscles, it is assumed that the area is *motor* in function—is an *area of motion*.

The animals generally employed for experiments of this character are dogs and monkeys, though other animals have frequently been employed by different investigators. Of all animals, the monkey is the most frequently selected, as the configuration of the brain in its general outlines more closely resembles that of man than does the brain of any other animal. The results therefore which are obtained, there is every reason to believe, are the results, in their general outlines, that would follow stimulation of the human brain if this were possible under the same conditions. Indeed, the clinical symptoms which arise during the development of pathologic processes, and the phenomena which occur during surgical procedures for the removal of growths and pathologic cortical areas, justify the conclusion that the chart of the sensor and motor areas of the monkey brain may be transferred to the human brain without introducing any serious errors.

The Sensor and Motor Areas of the Monkey Brain.—From experiments made on the brains of monkeys, Ferrier, Schäfer, Horsley, and many others have mapped out, though not with a high degree of definiteness and certainty, a number of areas, stimulation of which gives rise to sensation, while their destruction is followed by a loss of sensation on the opposite side of the body. Collectively these areas are known as sensor areas and are as follows:

1. A tactile area or an area for tactile sensibility.
2. An olfactory and a gustatory area or areas for olfactory and gustatory sensibility.
3. An auditory area or an area for auditory sensibility.
4. A visual area or an area for visual sensibility.

These same investigators have mapped out a number of other areas, stimulation of which gives rise to contraction of muscles on the opposite side of the body producing movements which are so coördinate and purposive in character that they may be regarded as identical with those produced by volitional effort, while destruction of these areas is followed by a loss of motion or paralysis of these muscles. Collectively these areas are known as motor areas and are as follows:

1. A head and eye area.
2. A face area.
3. An arm area.
4. A trunk area.
5. A leg area.

The location of these areas will be apparent from an examination of Figs. 248 and 249.

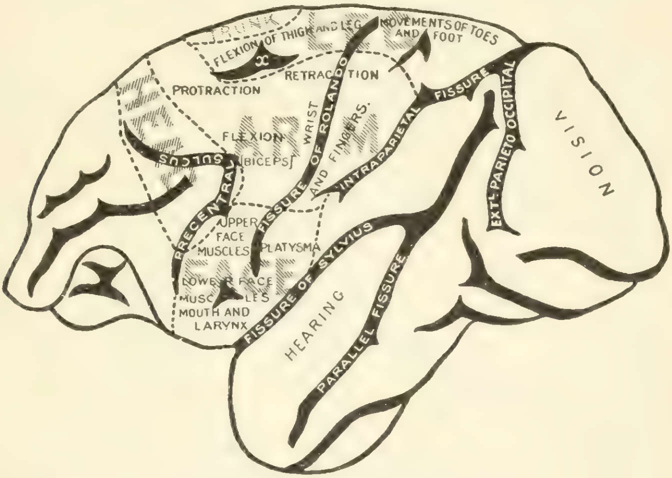
TRUNK
LEG
FLEXION OF THIGH AND LEG
MOVEMENTS OF TOES AND FOOT
RETRACTION
PROTRACTION
ARM
FLEXION
(BICEPS)
WRIST
AND FINGERS.
SULCUS
PRECENTRAL
FISSURE OF ROLANDO
INTRAPARIETAL FISSURE
EXT. PARIETO OCCIPITAL
VISION
UPPER FACE MUSCLES
PLATYSMA
FACE
LOWER FACE MUSCLES
MOUTH AND LARYNX
FISSURE OF SYLVIUS
HEARING
PARALLEL FISSURE

FIG. 248.—DIAGRAM OF THE MOTOR AND SENSOR AREAS ON THE LATERAL SURFACE OF THE MONKEY BRAIN.—(*After Horsley and Schäfer.*)

Motor Reactions Following Electric Stimulation of Sensor Areas.—Electric stimulation of the sensor areas is attended by certain motor reactions which vary in accordance with the area stimulated. Thus, when the electrodes are applied to different portions of the occipital lobe the eyeballs are conjugately turned upward, downward, or laterally and to the opposite side; when placed on the upper portion of the superior temporal convolution, the ear is pricked up or retracted, the head is turned to the opposite side and the pupils are dilated; when placed on the hippocampal convolution, there is movement of torsion of the nostril and lips of the same side. It was then assumed that the movements were reflex in character inasmuch as they resembled the movements caused by strong impressions made on the sense-organs, and due to the development of sensations by the electric currents and not an evidence that the area in question is a motor area in the sense that this term is applied to the area along the Rolandic fissure especially as their destruction is not followed by paralysis of any of the corresponding muscles. The view that these reactions are reflex in character has been substantiated by the anatomic fact that in the immediate neighborhood of each sense area, though not overlapping it, motor cells are present from which efferent nerve-fibers pass in close relation to the afferent fibers, toward and to lower nerve-centers and presumably to the centers of origin of related cranial nerves. This interpretation is supported by the experiments of Schäfer, which showed that the contraction of the eye muscles which followed stimulation of the occipital lobe took place between 0.2 and 0.3 second later than when the frontal lobe was stimulated; and that as the motor reaction takes place after extirpation of the frontal region, the route of the efferent impulse cannot be to and through the frontal lobe, but probably through some lower center. The same facts hold true for the reactions of the ear muscles following stimulation of the temporal lobe.

For these reasons it came to be believed that each sense area is associated with a motor area, though the two are not identical but separate in their distribution. The associated motor areas assist in the formation of a mechanism by which reflex movements are executed when sense organs are stimulated.

The view that the cortex of the cerebrum can be divided into separate and independent though physiologically related motor and sensor areas has, however, been questioned in recent years, and a somewhat different interpretation given to the facts. It is believed by many physiologists and neurologists that the so-called motor and sensor areas are so closely related that it is almost impossible to distinguish one from the other either anatomically or physiologically. Thus the Rolandic region is believed to be both motor and sensor in function, the former, however, being more predominant in the precentral, the latter in the post-central, convolution. As these two functions are so intimately blended and their anatomic substrata so difficult of separation, it is thought the term *sensori-motor* should be employed as more descriptive and more in accordance with the facts to the entire Rolandic region.

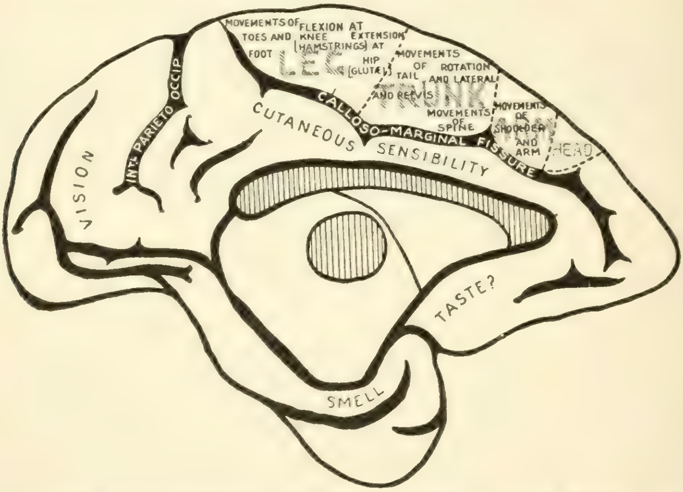
MOVEMENTS OF TOES AND FOOT
FLEXION AT KNEE (HAMSTRINGS)
EXTENSION AT HIP (GLUTEI)
LEG
MOVEMENTS OF TAIL AND PELVIS
ROTATION AND LATERAL MOVEMENTS OF SPINE
TRUNK
MOVEMENTS OF SHOULDER AND ARM
ARM
HEAD
INT. PARIETO OCCIP.
CALLOSO-MARGINAL FISSURE
CUTANEOUS SENSIBILITY
VISION
TASTE?
SMELL

FIG. 249.—DIAGRAM OF THE MOTOR AND SENSOR AREAS ON THE MESIAL SURFACE OF THE MONKEY BRAIN.—(*After Horsley and Schäfer.*)

This view has been strengthened by the results of the embryologic investigation of Flechsig, which show that different nerve-tracts become medullated or receive their myelin investment at successively later periods and that the tracts which first become myelinated and are hence first functionally active, belong to the afferent system. Among the first to undergo myelinization are three tracts numbered by Flechsig 1, 2 and 3, which arise largely from the median nucleus of the thalamus and the medial lemniscus and pass to the anterior and posterior convolutions, to the para-central lobule and foot of the superior frontal convolution, and to the foot of the third frontal convolution respectively. It is these fibers which convey nerve impulses to the cortex and furnish information regarding changes taking place in the body itself and thus lead to the performance of muscle movements. This area is therefore primarily a sensor area, an area for body-feelings, cutaneous, tactile, muscle, and visceral, and secondarily a motor area. The afferent fibers to this region become myelinated during the ninth month of intra-uterine life, the efferent fibers from it become myelinated during the third month of extra-uterine life.

By the same method of reasoning the gustatory, olfactory, auditory, and visual sense areas are to be regarded as sensori-motor in character, for embryologic investigations show that subsequently to the myelinization of the afferent tracts connecting the sense-organs with the cortex, efferent nerve-tracts arise from or near to the same centers and undergo myelinization. In other words, these areas are primarily sensor and secondarily motor, and therefore should be termed sensori-motor. In Flechsig's own terminology each *corticopetal* or afferent tract is accompanied by a *corticofugal* or efferent tract.

The view, viz.: the coincidence of sensor and motor areas has had general acceptance for the reason that it seemed more in accordance with the facts than the earlier view. Nevertheless there were many facts both of a physiologic and pathologic character which were difficult to harmonize with it, and in recent years the accumulation of facts and the weight of evidence inclines toward the view that the areas are anatomically separate and distinct though associated functionally.

The Motor Area of the Chimpanzee Brain.—In a series of experiments made by Sherrington and Grünbaum on the brain of the chimpanzee it was discovered that the so-called motor area was not so widely distributed as in the monkeys generally, but was confined almost exclusively to the convolution just in front of the fissure of Rolando, as it was impossible to obtain any movement on direct stimulation of the convolution just behind it. All points on the surface of the pre-central convolution, including the portion forming the wall of the Rolandic fissure itself, were found to be excitable and productive of movement when stimulated. The sequence of representation from below upward is similar to that observed in the monkey. One peculiarity, however, was the location of the area for conjugate deviation of the eyeballs to the opposite side. This is situated far forward in the middle and inferior frontal convolutions, and separated from the areas in the pre-central convolution by a region apparently inexcitable. These facts are of great interest and value in the assignment of the motor areas in the cortex of the human brain, as in its development and configuration the chimpanzee brain more closely resembles the human brain than does the monkey's.

The Localization of Sensor and Motor Areas in the Human Brain.—The observation of clinical symptoms and their interpretation by post-mortem findings, the phenomena observed during surgical procedures, and the results of embryologic investigations, point to the conclusion that corresponding areas both for sensations and movements exist in the cerebral cortex of the human brain, though it is probable that their locations do not in all respects coincide with those characteristic of the monkey or even the ape brain. In the following diagrams (Figs. 250 and 251), the sensor and motor areas are at least provisionally located, in accordance with recent observations. They are represented as limited or bounded by a serrated line to indicate, as suggested by Mills, that they are not sharply delimited, but that they interfuse or interdigitate with surrounding regions.

In the following paragraphs these areas are considered in the order of their development and physiologic activities.

The Sensor Areas.—The sensor areas occupy regions corresponding in a general way with those of the monkey brain.

1. *The Cutaneous Area.*—The area of cutaneous or tactile sensibility has been assigned to the post-central convolution on the lateral aspect, and to a portion of the super-frontal convolution and the lower half of the para-central lobule on the mesial aspect of the hemicerebrum. It has been stated by Flechsig, who bases his statements on the results of embryologic investigations as to the course, time of myelinization and termination of certain afferent tracts, that the cutaneous area must also be assigned though perhaps in less degree to the pre-central convolution as well.

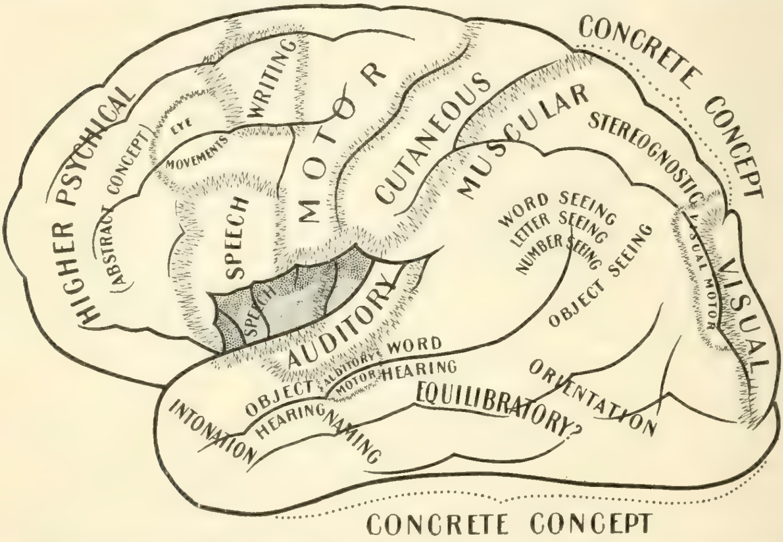
HIGHER PSYCHICAL
(ABSTRACT CONCEPT)
EYE
MOVEMENTS
WRITING
SPEECH
MOTOR
CUTANEOUS
MUSCULAR
CONCRETE CONCEPT
STEREOGNOSTIC
WORD SEEING
LETTER SEEING
NUMBER SEEING
OBJECT SEEING
VISUAL MOTOR
VISUAL
SPEECH
AUDITORY
AUDITORY WORD
MOTOR
HEARING
OBJECT
HEARING
NAMING
INTONATION
EQUILIBRATORY?
ORIENTATION
CONCRETE CONCEPT

FIG. 250.—THE AREAS AND CENTERS OF THE LATERAL ASPECT OF THE HUMAN HEMICEREBRUM.—(*C. K. Mills.*)

Clinic observations and post-mortem findings, together with the results of more recent experimental investigations make it extremely probable that the cutaneous area is confined entirely to the regions posterior to the central fissure or fissure of Rolando. Dr. Charles K. Mills, whose skill in interpreting the phenomena of the diseases of the brain is well known, states in this connection, that "innumerable cases have been reported of lesions of the motor (the pre-central convolution) without the slightest impairment of sensibility." In many instances portions of the motor cortex of the human brain have been excised by necessary surgical procedures. In these cases also, careful studies have failed to show any impairment of sensibility. On the other hand, destruction of the post-central convolution in monkeys by the electro-cautery and in man by disease has invariably led to a loss of sensibility, hemianesthesia, on the opposite side of the body without at the same time causing any loss of motion. The location and extent of the anesthesia corresponds, of course, with the location and extent of the lesion of the cortex.

Cushing has recently recorded the results of stimulation with the electrical current of the post-central convolution in two conscious patients. The localized stimulus gives rise to definite sensations which were likened in one case to a sensation of numbness, and in the other to a definite tactual impression. From the foregoing facts it may be stated in a general way that the post-central convolution is the region for tactile (light touch) and associated forms of sensation such as tactile discrimination and localization and perhaps of the finer shades of temperature, in other words of epi-critic sensibility.

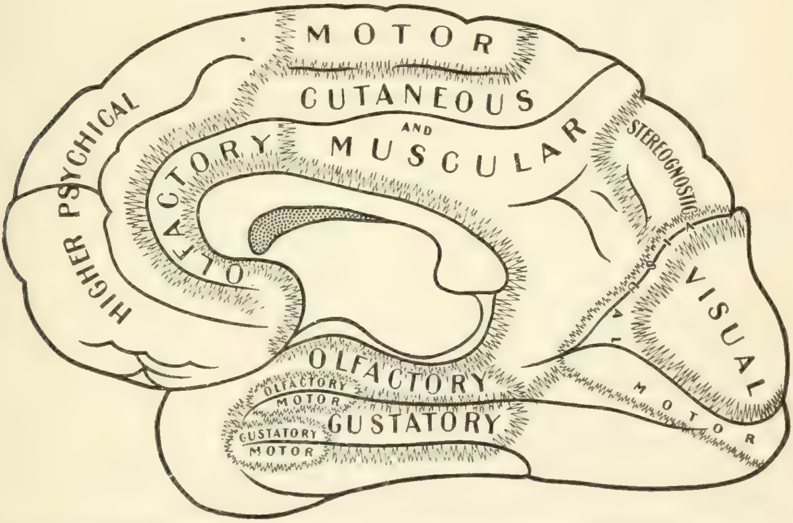

FIG. 251.—THE AREAS AND CENTERS OF THE MESIAL ASPECT OF THE HUMAN HEMICEREBRUM.—(*C. K. Mills.*)

2. *The Muscle Sense Area.*—The area of muscle sensibility has been assigned to the region posterior to but adjoining the post-central convolution and includes the anterior part of the super-parietal and sub-parietal convolutions and perhaps the supra-marginal convolution on the lateral aspect and a portion of the callosal convolution on the mesial aspect of the hemicerebrum.

The sensations which are evoked in response to the action of nerve impulses coming from tendons, muscles, etc., are those of passive position and the direction and duration of movements of parts of the body. Clinic observations and post-mortem findings indicate that lesions of this area are followed by a loss of the muscle sense. Owing to the close juxtaposition of the areas of cutaneous and muscle sensibility it is unusual to find a loss of muscle sense without impairment of the tactile sense, not infrequently they coexist. Surgical removal of a small angioma posterior to the post-central convolution and about the junction of the super- and sub-parietal convolutions was followed by a loss of the muscle sense in the opposite hand and forearm without any disturbance of other sensations (Starr and McCosh). In addition to sensations of passive position and direction of movements, the sensations of temperature and deep pressure are also associated with the physiologic activities of this region of the parietal lobe. There is much obscurity as to the location, however, of the area in which sensations of pain are evoked. These two areas together constitute the area of the body-feelings or the *someaesthetic* area.

Subdivisions of the Cutaneous and Muscle Sense Areas.—Clinic observations and post-mortem findings also warrant the deduction that the general areas of cutaneous and muscle sense areas are physiologically subdivided as is the general motor area (see page 590) into areas for the skin and muscles of the face, arm, trunk, and leg which occupy respectively areas that adjoin the corresponding subdivisions of the motor area representing these parts of the body (Mills). On the mesial surface of the cerebrum there are sensor areas for a portion of the leg, anus, genitalia and viscera.

The afferent pathway through which the nerve impulses, developed in the sense-organs of the skin, tendons and muscles, pass to the cortical areas and evoke the characteristic sensations has been described on pages 544 and 545.

3. *The Stereognostic Area.*—The area of stereognostic perception. Stereognosis is the recognition of an object when placed in the hands, through its form, density, temperature, etc. The area associated with stereognostic perception has been assigned to a portion of the super-parietal convolution and to the precuneus.

This perception depends on the integrity and coöperation of the tactile, the pressure, the temperature and muscle senses as well as the power of discriminating points in contact with the skin. A lesion of this area impairs or destroys the power of recognition of objects and establishes the condition of *astereognosis.* This judgment, however, would also be impaired or abolished if either the tactile or muscle sense were impaired or abolished, since both are necessary factors in the series of events that lead to the formation of the judgment. The existence of such a center has been made highly probable by clinical cases in which astereognosis existed without impairment of either the cutaneous or muscle sensibility. Inasmuch as focal lesions of the parietal cortex give rise to localized impairment of stereognostic perception as well as impairment of the cutaneous and muscle senses, it is stated that the area is also capable of subdivision into smaller areas for the face, arm, trunk and leg (Mills).

4. *The Gustatory Area.*—The area for gustatory sensibility has been assigned to the sub-collateral convolution on the mesial aspect of the temporo-sphenoidal lobe.

Disease processes involving this area give rise frequently to subjective sensations of taste. Electric stimulation of this area in mammals causes movements of the lips, tongue, etc., which are usually associated with sensations of taste.

The afferent pathway by which nerve impulses, developed by action of organic matter in solution on the terminal portions of the gustatory nerves, are transmitted to the cortical area is considered in connection with the sense of taste.

5. *The Olfactory Area.*—The area for olfactory sensibility has been assigned to the anterior portion of the hippo-campal convolution (the uncinate region) and the anterior portion of the callosal convolution or gyrus fornicatus.

Disease processes in this region give rise frequently to subjective sensations of odors which as a rule are of an unpleasant character. Destruction of this area is followed by a loss of odor sensations. Electric stimulation of this area in mammals was found by Ferrier to be attended with a peculiar torsion of the nostril and lips on the same side similar to the reaction brought about by the application of an odorous substance more or less disagreeable to the nostril.

The afferent pathway, by which nerve impulses developed in the terminal portion of the olfactory nerve by the contact of odorous particles are transmitted to the cortical areas, is considered in connection with the olfactory nerve.

6. *The Auditory Area.*—The area of auditory sensibility has been assigned to portions of the temporal lobe and may be divided into primary and secondary areas.

   The primary area is located in the posterior portion of the super-temporal convolution, and perhaps the posterior portion of the insula. The secondary areas are located one below and in advance, and the other below and some what behind the primary area, both extending into the medi-temporal convolution.

Unilateral destruction of the primary area is followed, however, only by a partial loss of hearing in the opposite ear, owing to partial decussation of the auditory nerve, which, however, may be recovered from, after a time, owing probably to a compensatory activity of the insular convolution. Bilateral destruction of this region is followed by complete deafness. The primary area is connected on the one hand with the basal auditory center (the internal geniculate body) by the auditory radiation, and on the other hand with the secondary areas by association fibers.

In the first of these areas there are cells in which the sounds of objects are registered (object hearing); in the second of these areas there are cells in which the sounds of words, letters, etc., are registered or memorized. If these areas are destroyed by disease the condition of *object-deafness* and *word-deafness* is established. If word-deafness alone exists, the patient though able to recognize sounds is unable to understand spoken language and is in the condition of a man who is hearing a language of which he has not the slightest idea. The same holds true for the perception of sensations of sound produced by objects.

The afferent pathway by which nerve impulses, developed in the terminal portions of the auditory nerve by the impact of atmospheric vibrations are transmitted to the auditory area, is considered in connection with the consideration of the auditory nerve and tracts.

In the temporal lobe there are other areas, some of which are more or less associated with the auditory nerve, such as intonation, equilibratory and orientation areas. In the subtemporal and probably in the medi-temporal convolution as well, there is an area in which, it is believed by some clinicians, words are associated with concrete ideas of objects recognized by one or more of the senses. To this area the term *naming area* has been given. It is connected by association fibers with the areas for word hearing and word seeing.

7. *The Visual Area.*—The area for visual sensibility has been assigned to portions of the occipital and parietal lobes and may be divided into primary and secondary areas.

   The primary area is located in a triangular-shaped area on the mesial surface of the occipital lobe, which includes the gray matter between the parieto-occipital and the calcarine fissures (the cuneus), and in the gray matter of the first occipital convolution on the lateral aspect of the occipital lobe. The secondary areas are located partly on the lateral aspect of the occipital lobe and partly in the supra-marginal and angular convolutions of the parietal lobe.

Focal lesions of the primary area on one side are followed by lateral homonymous hemianopsia, which, however, does not involve, as a rule, the fovea or macula.[1] It is, therefore, the area of homonymous half-retinal representation. The location of the area for macular or central vision is uncertain. Henschen locates it in the anterior part of the area near the extremity of the calcarine fissure, and asserts that in each area both maculæ are represented. From experiments made on monkeys Schäfer locates it in the same region.

The primary area is connected, on the one hand, with the basal visual centers (the external geniculate body and the thalamus) by the optic radiation and, on the other hand, with the secondary areas by association fibers.

The secondary areas on the lateral aspect of the occipital lobe are rather extensive, reaching down as far as the third and fourth occipital convolutions. Clinical evidence indicates that the cortex of this entire area is associated with the registration or memorization of the visual sensations and perceptions of objects, though it may be subdivided into smaller areas for the registration of the visual sensations of different groups of objects such as geometric and architectonic forms, of persons, places and natural objects. Diseased processes in this region of the brain may result in the condition known as *object blindness*. The area on the lateral aspect of the parietal lobe (the supramarginal and angular convolutions) are associated with the memorization of the visual sensations and perceptions of words, letters, numbers, and perhaps objects. If the visual word area is destroyed by disease, *word blindness* is established, and the patient is unable to understand written or printed language because of his inability to revive memory images of words. *Letter* and *number blindness* may or may not be present according to the extent of the lesion.

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[1] In a consideration of this subject certain facts connected with visual perception, both in physiologic and pathologic conditions, must be kept in mind. Thus, visual sensation may arise from stimulation of either the central portion, the macula, or the peripheral portion of the retina or both. In the first instance the vision is termed central or macular; in the second instance, peripheral or retinal. Macular vision is clear, sharp, and distinct; retinal vision progressively indistinct from the center toward the periphery. Division of one optic tract is followed, in consequence of the partial decussation of the optic nerve-fibers at the chiasma, by a loss of function in the outer two-thirds of the retina of the same side, both in the central (macular) as well as in its peripheral portions, and the inner one-third of the retina of the opposite side. To this condition the term hemianopsia has been applied. As a result of this want of functional activity of these retinal portions on the side of the lesion, rays of light emanating from objects situated in the *opposite side* of the *field of vision* will not be perceived when both eyes are directed to the fixation point. To this "blindness" in the opposite half of the field of vision the name hemianopsia is given. In the lesion under consideration (division of one optic tract) the hemianopsia is *bilateral*, and as it affects the corresponding portions associated in normal vision it is of the *homonymous* variety. Division of the right optic tract is followed by *left lateral homonymous hemianopsia*, indicative of the fact that objects in the field of vision to the left of the binocular fixation point are invisible.

All the special sense areas may, therefore, be said to consist of two smaller areas, a *sensor* and a *psychic*, *e.g.*, a cutaneous sensor and a cutaneous psychic, a visual sensor and a visual psychic, etc.; the former is for the development of crude sensation; the latter, more complex in character, is for the correlation and formation of sensations whereby judgments or definite conceptions are formed (Campbell).

The Sensori-motor Areas.—It will be observed on examination of diagrams 250 and 251, that each sense area has closely associated with it a sense motor area, each of which is to be regarded, from one point of view at least, as a constituent part of the motor area of the cortex.

On a previous page it was stated that electric stimulation of sensor areas is attended with certain motor reactions in the muscle groups associated with the activities of the sense-organs, reactions which resemble those caused by strong impressions made on the sense-organs by external agents; that some investigators, therefore, believed that the areas in question were motor and sensor in function and that their anatomic substrata were so intermingled and so difficult of separation that the term *sensori-motor* should be employed as more descriptive and more in accordance with the facts; but that the progress of experimental work, together with the accumulation of facts from the clinical and pathologic fields, incline to the view that the groupings of the motor and sensor cells are anatomically and physiologically separate and distinct though related functionally. Corresponding areas are now believed to be present in the human brain. For this reason each of the special sense areas, with the exception of the cutaneous, is represented in Fig. 250, as associated with a motor area, viz.: a gustatory, an olfactory, an auditory and a visual motor area. The cutaneous sensor area is, however, also associated with a cutaneous motor area in the posterior portion of the pre-central convolution. These associated motor and sensor areas are here represented, not as overlapping, but contiguous, though perhaps interdigitating with each other. Their location and relations are apparent from an examination of the diagrams. From the results of experimental investigations it is generally believed the sense motor areas are more particularly related to *sensori-motor* reflex actions rather than to voluntary actions and that they constitute the efferent element of a reflex arc, since destruction of the area interferes with the former rather than the latter.

It will be recalled that the investigations of Flechsig demonstrated that from these areas efferent or motor nerves pass through the sense tracts or radiations in the reverse way, to the mid-brain, where they become related to the nuclei of origin of the motor cranial nerves which excite to action those muscles associated with the sense organs in their adjustments to the stimulus. Thus electric stimulation of the gustatory motor area gives rise to movements of the lips and tongue; of the olfactory motor area, to movements of the nostrils, etc., as in sniffing; of the auditory motor area to movements of the head and eyes to the opposite side and to pricking of the ears; of the visual motor area to movements of the eyeballs and head in different directions, in accordance with the part stimulated. All these movements are similar to those which follow gustatory, olfactory, auditory, and visual sensations, evoked by unexpected stimulation of the peripheral sense-organs themselves.

The Motor Areas.—The motor areas especially those associated with the execution of volitional movements have been assigned to the pre-central convolution, the contiguous portions of the base of the medi- and sub-frontal convolutions and the para-central lobule.

The exclusion of the post-central convolution from the motor area, to which it belongs in the monkey brain, is in accordance with the embryologic researches of Flechsig, which indicate that the efferent fibers which compose the pyramidal tract come from the region anterior to the central fissure, and with the experiments of Sherrington and Grünbaum on the brain of the chimpanzee, which demonstrate that the post-central convolution is absolutely inexcitable to electric stimulation. It is quite probable that with the growth of the brain in size and complexity, the motor area has come to occupy a position somewhat farther forward in the human brain than in the monkey brain.

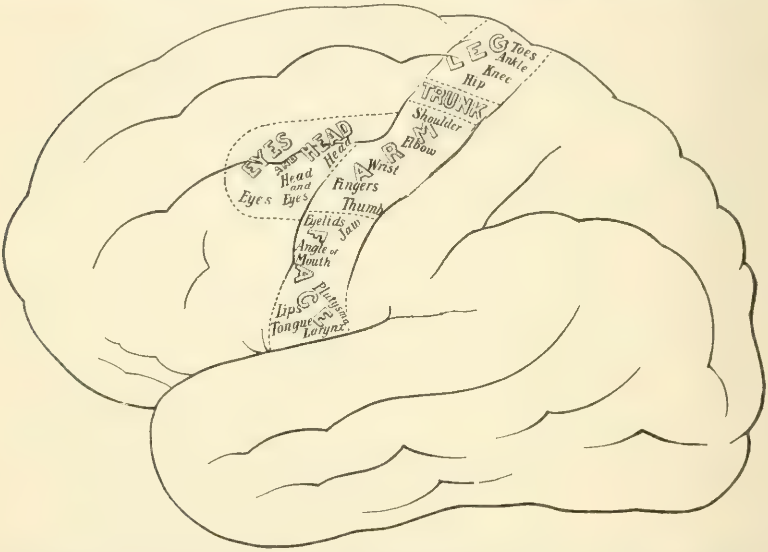

FIG. 252.—SCHEME OF THE MOTOR AREA OF THE HUMAN BRAIN AND ITS SUBDIVISIONS.—(*After Mills.*)

This general area is capable of subdivision into areas of variable size, *e.g.*, head and eyes, face, arm, trunk, and leg areas which are related through the efferent nerve-fibers composing in part the pyramidal tract to groups of muscles, *e.g.*, head and eye muscles, face, arm, trunk and leg muscles, on the opposite side of the body and the activities of which they initiate and control. (See Figs. 250 and 252.)

These large subdivisions of the cortical motor area are in turn capable of a further subdivision into smaller areas which are in relation with one or more muscles of the larger groups. These smaller areas indicated in the diagram by compressed italics contain groups of nerve-cells which excite to action, through their efferent axons and their medullary and spinal connections, the muscles which impart movements to the regions corresponding to the words in compressed italics.

The main motor areas are as follows:

1. *The Head and Eye Area.*—This area has been assigned to the contiguous portions of the medi- and sub-frontal convolutions just anterior to the pre-central convolution. It is subdivided into smaller areas which initiate and govern the movements of the head and eyeballs. Stimulation of this area, in the chimpanzee at least, produces turning of the head to the opposite side with conjugate deviation of the eyes to that side.
2. *The Face Area.*—This area has been assigned to the lower portion of the pre-central convolution and extends from below upward to about the level of the genu of the central fissure. This rather large area may be subdivided into (*a*) an upper portion including about one-third of the whole and (*b*) a lower portion including the remaining two-thirds. In both the upper and lower portions, there are groups of nerve-cells which excite to action the muscles imparting movements to (*a*) the angle of the mouth, the eyelids and jaws and (*b*) the movements of the vocal bands or cords, the opening and closing of the mouth, the protrusion and retraction of the tongue. All of these movements have their areas of representation in the face area.
3. *The Arm Area.*—This area has been assigned to the pre-central convolution just above and contiguous to the face area which it exceeds somewhat in extent. It is the largest of all the subdivisions of the general area. It may be divided into at least five smaller areas, the cells of which excite to action the muscles imparting movements to the thumb, the fingers, the wrist, the elbow and the shoulder.
4. *The Trunk Area.*—This area has been assigned by Sherrington and Greenbaum to the pre-central convolution just superior to the arm area and is rather limited in extent. Horsley located a portion of this area on the mesial and lateral edges of the hemisphere in front of the leg area. The nerve-cells of this area when electrically stimulated excite to action the muscles which impart movements to the spinal column, such as arching rotation, etc.
5. *The Leg Area.*—This area has been assigned to the extreme upper portion of the pre-central convolution and to the adjoining mesial surface, the upper portion of the para-central lobule. The area on the lateral aspect of the cerebrum may be subdivided into at least four smaller areas containing groups of nerve-cells which excite to action the muscles imparting movements to the toes, ankle, knee and hip.

Evidence from the clinical side has demonstrated the fact that a *localized irritative lesion* of any one of these areas gives rise to convulsive movements of the muscles of the opposite side of the body, similar in character to those resulting from electric simulation of the corresponding areas of the monkey and ape brains. *Destruction* of these areas from the growth of tumors, softening, etc., is followed by paralysis of the muscles. Electric stimulation of these areas of the human brain for the purpose of localizing obscure irritative lesions prior to surgical procedures on the brain gives rise to similar convulsive movements.

The motor speech and the motor writing areas will be considered the following paragraphs.

Language.—Language may be defined as the expression of ideas by a succession of motor acts and may be divided into (1) spoken language (articulate speech), and (2) written language. The expression of ideas by words (speech) and by verbal signs (writing) depends primarily on the power of reviving images or memories of objects, words, letters, numbers, etc., seen and heard, and secondarily on the power of reviving the images or memories of the muscle movements which were previously employed in an effort to imitate or reproduce the sounds of objects, words, letters, etc. (speech) or the visual impressions by verbal signs (writing).

For both spoken and written language two phases of activity are to be recognized, viz.: a receptive or sensor and an emissive or motor.

1. **The Receptive or Sensor Phase.**—Before language can be acquired by a developing child, impressions of external objects must be made on the visual, auditory and other sense-organs as well, which in consequence lead to the development in the corresponding cortical areas of sensations and ultimately of conceptions regarding the nature of the objects impressing themselves on the peripheral sense-organs.

   Thus, through the visual apparatus in its entirety, definite concrete conceptions regarding the shape, size, color, etc., of an object or word, letters and numbers, etc., are obtained. For future use the sensations must not only be perceived but registered or memorized. The memorization of the sensations produced by luminous objects, is supposed to be associated with the activities of the cortex on the lateral aspect of the occipital lobe; the sensations produced by words, letters, and numbers with the activities of the cortex of the supra-marginal and angular convolutions of the parietal lobe. This is made possible by means of association fibers which unite the primary visual area in and around the cuneus, with the secondary visual areas. That the visual memories are associated with the previously mentioned convolutions of the parietal and occipital lobes is apparent from the fact, that if they are destroyed by disease there is a loss of these memories even though the individual sees the objects as formerly; but though seeing them they cannot be remembered or recalled. To this condition the terms *word* and *object blindness* have been given.

Coincidently with the development of visual sensations and their memorization, the child receives through the auditory apparatus in its entirety, definite concrete conceptions regarding the intensity, pitch and timbre or quality of sounds produced by atmospheric vibrations, due to vibrating bodies; sounds which are subsequently associated with the vocal and articulating apparatus of human beings when pronouncing words, letters and numbers, or with objects such as bells, musical instruments, etc. For future use the sensations thus aroused must not only be perceived but likewise registered or memorized. The memorization of the sensations produced by atmospheric vibrations is supposed to be associated with the activities of the temporal lobe and more particularly of the posterior two-thirds of the super-temporal and medi-temporal convolutions. This is made possible by means of association fibers which unite the primary auditory area with the secondary auditory areas. That the auditory memories are associated with the previously mentioned convolutions is apparent from the fact that if they are destroyed by disease, there is a loss of these memories even though the individual hears the sounds as formerly, but though hearing them, they cannot be remembered or recalled. To this condition the terms *word deafness* and *object deafness* have been given.

From the concrete conceptions formed of individual objects of a similar character or of a class, there are developed abstract conceptions, by the uniting into a single idea the elements which are common to all the objects of the class. This involves an analysis and a synthesis, a recognition of the points of similarity and dissimilarity. The development of abstract conceptions is believed to be associated with the activities of the cortex of one or the other of the association areas (see page 596).

For the emission of the sounds of words which constitute spoken language it is essential that the sensations produced by the muscle movements shall not only be perceived but registered or memorized. Without this the capacity to express words would not be possible. This registration is believed to be associated with the lower portion of the area for muscle sensibility.

2. **The Emissive or Motor Phase.**—In an attempt to express ideas by spoken or written language the muscles determining the action of the larynx, jaws and teeth, tongue, lips, hands, etc., are excited to action by nerve impulses descending through nerves, the nuclei of origin of which lie in the gray matter beneath the floor of the medulla oblongata and in the gray matter of the spinal cord. The nuclei of these nerves are in turn excited to action by nerve impulses descending by way of the internal capsule from the cortical areas for the face and arm respectively.

The Motor Speech Area.—By this term is meant an area of the cortex, the function of which is to arrange language for outward expression; for the use of the executive centers concerned with speech, viz.: the laryngeal, lingual and facial centers located at the foot of the pre-central convolution. This area, *i.e.*, the motor speech area, has been assigned to the posterior part of the subfrontal convolution (Broca's convolution) on the left side in those who are right-handed and on the right side in those who are congenitally left-handed, and in the anterior part of the insular or perhaps the pre-insular convolutions. Unipolar faradic stimulation of this area fails to call forth any motor response; its destruction by disease, however, is followed by a more or less extensive loss of the faculty of articulate speech or the faculty of expressing ideas with words, a condition usually spoken of as motor *aphasia* or *aphemia*. This area and the area at the foot of the pre-central convolution are united by association fibers.

The Motor Writing Area.—By this term is meant an area of the cortex, the function of which is to arrange language for outward projection; for the use of the executive centers concerned with writing, viz., the arm centers located in the middle portion of the pre-cental convolution. This area, *i.e.*, the motor writing area, has been assigned to the posterior half or third of the medi-frontal convolution. Unipolar faradic stimulation of this area fails to call forth any motor response; its destruction by disease, however, is followed by an inability to express ideas by writing, a condition usually spoken of as *agraphia*. This area and the general arm center in the pre-central convolution are united by association fibers.

The Language Zone.—These different areas are connected with one another by association fibers, and, taken collectively, constitute the language zone, which in people who are congenitally right-handed is located on the left side of the brain only. Their situation and relations are shown in Fig. 253. In this figure the dotted lines coming from the eye (v) and ear (a) represent the visual and auditory tracts through which nerve impulses pass to the visual centers (V) and the auditory (A) respectively. Similar lines coming from the muscles involved in speech and writing might also be represented to indicate the paths of the nerve impulses to the muscle sense areas not shown in the diagram. The single continuous lines on the surface of the cortex represent nerve-fibers which associate the visual and auditory centers with the speech and writing centers. The double lines associate the visual and the auditory areas with the frontal association area on the one hand and the association area with the motor speech and the motor writing area respectively. The dotted lines coming from the speech and writing centers represent the tracts coming from the areas in the pre-central convolutions, and through which nerve impulses pass to the muscle of the larynx, tongue, mouth, and lips, and to the muscles of the hand. The anatomic and physiologic association of the various areas is essential to the registration of the impressions made on the ear and eye and for the expression of the ideas evolved from them by words (speech) and signs (writing). Their collective action is essential to the acquisition of language. Destruction of any part of this cerebral mechanism is attended by an impairment of or a total loss in either the power of obtaining auditory images of words heard and visual images of words seen, or the power of expressing ideas by speech and writing. To this pathologic condition the term aphasia has been given.

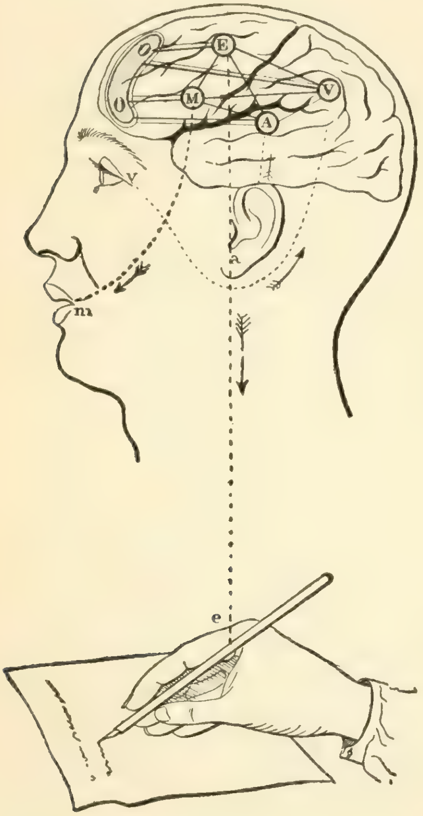

Fig. 253.—Diagram Showing the Relation of the Centers of Language and their Principal Associations. A. Auditory center. V. Visual center. M. Motor speech center. E. Motor writing center. O O. Intellectual center.—(*After Grasset.*)

Aphasias are of many degrees and kinds, though they may be included in the two general divisions, *motor* and *sensor*.

Motor aphasia may be either aphemic or agraphic. In *aphemic* aphasia the patient is unable to express or communicate his thoughts by spoken words, owing to an inability to arrange words for outward expression and hence to execute those movements of the mouth, tongue, etc., necessary for speech without there being any paralysis of these muscles. The lesion is usually in the third frontal convolution and most frequently associated with right hemiplegia. In *agraphic* aphasia the patient is unable to communicate his ideas by writing through an inability to arrange verbal signs for outward expression and hence to execute the movements of the hand and arm necessary for writing. In this form of aphasia the lesion is in the writing area, in the posterior half or third of the medi-frontal convolution. These two forms of motor aphasia are not infrequently associated.

Sensor aphasia or amnesia may be either visual or auditory. In *visual* aphasia or amnesia the patient is unable to recognize a letter or word, printed or written (though capable of seeing other objects), a condition known as *letter* or *word blindness*. It is usually associated with lesions in the neighborhood of the supra-marginal convolution. In *auditory* aphasia or amnesia the patient cannot understand articulate or vocal speech, though capable of hearing and understanding other sounds, through an inability to distinguish the associations of words and letters—a condition known as *word deafness*. It is associated with lesions of the auditory area.

Paraphasia is an inability to recall the proper words to associate with ideas and necessary to their expression.

Concept aphasia is the inability to recall the names of objects. It is associated with lesions of the cortex of the mid-temporal or third temporal convolution (Mills). This area is known as the *concept* or *naming* area.

Many other forms of aphasia have been observed and described by clinicians which are fully considered in works relating to diseases of the nerve system.

The statements regarding the mechanism of speech, the functions assigned to the motor speech area (Broca's convolution) and the motor writing area, though very generally accepted, have been questioned in recent years by Marie who on the basis of clinico-pathologic facts has presented a somewhat different view which has found many adherents.

Marie's Theory of Aphasia.—Marie states that there is but one aphasia and but one speech center, which he locates somewhere in the left temporo-parietal lobe, and which he designates as a specialized intellectual center for speech. Motor aphasia in the accepted sense, he states, is a combination of word blindness and word deafness (both, however, being defects of the speech center) and defective articulation (anarthria) the result of a lesion of the motor tracts necessary to the excitation of the muscles for articulation. The lesion causing the anarthria is in the *lenticular zone*, in close relation to the lenticular nucleus. This zone, in a horizontal section of the brain, is limited anteriorly by a vertical plane level with the anterior sulcus of the insula, posteriorly by a similar plane level with the posterior sulcus of the insula; internally by the lateral ventricle and externally by the surface of the insula. This zone is anatomically associated with the supra-marginal and angular convolutions and with the posterior portions of the super- and medi-temporal convolutions which together constitute Wernicke's zone. In this view the distinction between motor and sensor aphasia, the functions assigned to the sub-frontal and medi-frontal convolutions and the existence of four speech centers are all rejected. Many published facts support this view though many others are at variance with it.

Bilateral Representation.—Though highly specialized movements, such as those performed by the arms and hands, legs and feet, have their areas of representation on one side of the cerebrum only, and that opposite to the side of the movement, less highly specialized movements, such as the masticatory, phonatory, respiratory and various trunk movements, which require for their performance the coöperation of muscles on both sides of the body, have their areas of representation on both sides of the cerebrum; the area of either side exciting to action the muscles on both sides of the body. In the case of specialized movements the representation is *unilateral;* in the case of the more general movements the representation is *bilateral.*

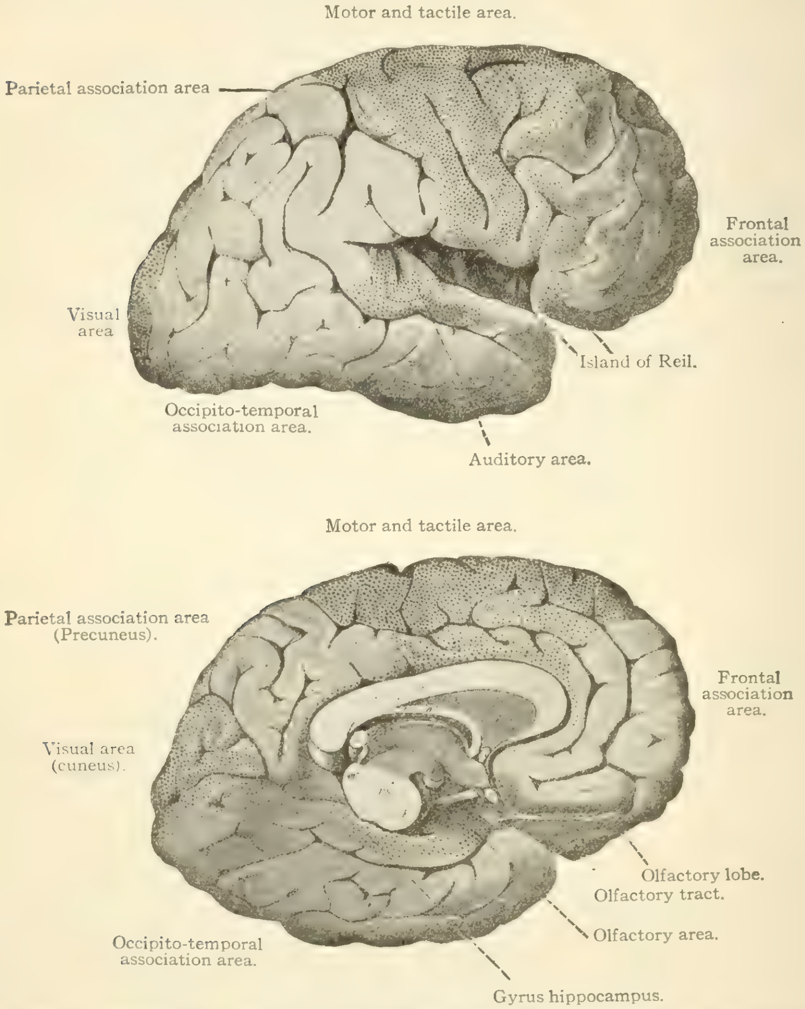
Motor and tactile area.
Parietal association area
Frontal association area.
Visual area
Island of Reil.
Occipito-temporal association area.
Auditory area.
Motor and tactile area.
Parietal association area (Precuneus).
Frontal association area.
Visual area (cuneus).
Olfactory lobe.
Olfactory tract.
Olfactory area.
Occipito-temporal association area.
Gyrus hippocampus.

FIG. 254.—DIAGRAMS TO SHOW THE POSITION AND THE RELATION OF THE ASSOCIATION AND PROJECTION AREAS. THE PROJECTION AREAS ARE DOTTED.—(*After Flechsig.*)

Association Centers.—The sensor and motor areas to which specific functions have been assigned do not constitute more than one-third of the total cerebral cortex. There yet remain large regions to which it has been impossible to assign specific functions based on physiologic experiments. Three or four such regions separated by the sensor and motor centers are to be recognized on the lateral and mesial aspects of the hemisphere. In Fig. 254 the location, extent, and names of these regions are represented. The fibers which are found in these regions belong almost exclusively to the association system, and become medullated at a later period than do the fibers of the projection system; moreover, from the method of their medullization it would appear that many of these fibers grow out directly from the sensor centers into these regions and become related to the nerve-cells of their convolutions, while others grow out from adjacent as well as distant convolutions. From histologic and pathologic evidence these regions were termed by Flechsig association centers or areas, implying the idea that through the intervention of their cell mechanisms the sense areas are indirectly associated anatomically and physiologically, and together constitute a mechanism by which sensations are associated and elaborated into concrete forms of knowledge or related to definite forms of movement.

It has been assumed by Flechsig that the *frontal association* center, from its connections with the sensor and motor areas of the Rolandic region, the olfactory, and perhaps other regions, is engaged in associating and registering body sensations and volitional acts, and that the knowledge thus gained has reference largely to the personality of the individual; that the *parieto-occipital* association area, from its relation to the visual, auditory, and tactile sense areas, is engaged in associating and registering visual, auditory, and tactile sensations, and that the knowledge thus gained has reference mainly to the external world. These assumptions in a general way are supported by the phenomena of disease. In certain lesions of the frontal lobe the symptoms indicate a loss or change of ideas regarding personality rather than of the objective world, while the reverse is true in disease of the parieto-occipital lobe.

The Intra-cranial Circulation.—The circulation within the cranium presents certain peculiarities which distinguish it from that in other parts of the body. These peculiarities reside in part in the anatomic arrangement of the blood-vessels, in the probable absence of vaso-motor nerves to the blood-vessels, and in greater part in the fact that the brain and its blood-vessels are contained in a case with rigid, unyielding, and closed walls.

The Blood-supply.—As stated in a previous paragraph the arteries supplying the brain with blood are four in number, viz.: the two internal carotids and the two vertebrals. These four arteries anastomose very freely at the base of the brain, the anastomosis constituting the circle of Willis. From this circle there arise the anterior, middle and posterior cerebral arteries which are distributed to the cortex and the underlying white matter. The basal ganglia, the capsule and adjacent white matter are supplied by a number of branches which arise from the circle of Willis or from the three cerebral arteries immediately after their origin. From the distribution of these two sets of vessels they have been named the cortical and the central ganglionic respectively.

The venous blood is returned by a system of vessels which present characteristics of physiologic interest. These vessels consist of large sinuses formed by folds of the dura mater or, as at the base of the cranium, by the dura mater and the bone. These sinuses, from the very nature of the tissues which enter into their formation, have rigid walls and will therefore withstand any pressure to which they may be subjected under physiologic conditions. The same obtains at their points of exit from the cranium where a free outflow is in consequence always assured.

The various sinuses have opening into them, the veins which return the blood from the cortex and subjacent white matter, and from the inner structures of the brain. Neither sinuses nor veins have valves and most of the veins which empty into the superior longitudinal sinus have their mouths directed forward, hence the blood discharged from these veins must flow against the current in the sinus. The venous blood leaves the cranium mainly by way of the internal jugular veins which are direct continuations of the lateral sinuses.

The Intra-cranial Lymph-spaces.—In order to understand the phenomena attending the circulation of blood through the cranium it is necessary to take into consideration an important fact, viz.: that the brain and spinal cord are surrounded on all sides by a relatively large and continuous lymph-space. This space which is found between the arachnoid and the pia mater is filled with a liquid, the so-called cerebrospinal fluid, which being interposed between the brain and the skull on the one hand and the spinal cord and the vertebræ on the other hand, acts as a water cushion protecting these delicate organs from the injury which might result from sudden jars. The ventricles of the brain are also filled with cerebrospinal fluid which is in communication with that in the subarachnoid space through the foramen of Magendie and the foramina of Key and Retzius. The cerebrospinal fluid may also penetrate into the perineural lymph-spaces surrounding the cranial and spinal nerves. The quantity of the cerebrospinal fluid is relatively small, amounting to from 60 to 80 c.c.

The Mechanism of the Intra-cranial Circulation.—As previously stated, by virtue of the physical relations existing between the blood, the brain, the cerebrospinal fluid and rigid walls of the cranium, the flow of the blood through the brain and cranial cavity, is attended by certain phenomena which are peculiar to this region and present in no other situation.

Taking as a point of departure the condition of the arteries during the cardiac diastole, the relations of these structures are somewhat as follows: the cerebrospinal fluid occupies all the available lymph-space, but under a pressure approximately equal to that in the large veins and hence not materially above that of the atmosphere; the pressure in the arteries, capillaries and veins presents the usual values in these different regions of the vascular apparatus; the brain presents a volume which may be termed diastolic.

With the occurrence of the succeeding cardiac systole, the cerebral vessels, receiving an additional volume of blood, expand and occasion a corresponding increase in the volume of the brain, which is accomplished by a partial displacement of the cerebrospinal fluid into extra-cranial lymph-spaces. Because of the fact that the displacement of the cerebrospinal fluid is insufficient to permit of the complete expansion of the brain, there is developed in the intra-cranial lymph-spaces a counter-pressure (the so-called intra-cranial pressure) which would keep pace with and finally equalize the rising pressure in the arteries. In consequence of this, the brain tissue, it is believed, would be subjected to a pressure sufficiently great to interfere with its activities, even to the point of unconsciousness. If this is not to occur the maximum expansion of the arteries, and hence the brain, must be checked and controlled. This is accomplished in the following way: As the brain approaches that degree of expansion permitted by the displacement of the cerebrospinal fluid, it begins to exert a compression of the pial veins. This compression by narrowing the lumen of the veins diminishes their capacity and hence increases the pressure of their contained blood until it is equivalent to the pressure exerted by the brain against the veins. At this moment the pressures in the arterioles, capillaries and veins approximate each other in value.

From these factors it will be seen that the circulation through the brain approximates a circulation through a system of rigid tubes. The result is an increase in the velocity of the outflow and a diminution of the blood-pressure. As an additional result the pulse-wave of the arterial system is transmitted to the blood of the large veins and sinuses which therefore exhibit normally pulsations synchronous with those of the arteries. The rise of the pressure in the cerebral veins is regarded therefore as the factor which, by limiting brain expansion, checks the rise of the intra-cranial pressure beyond physiologic limits. With the diastole of the heart and the recoil of the arteries, the former relation of the blood, brain, cerebrospinal fluid and cranial walls is regained. Because of this change of relation with each heart-beat, the brain pulsates synchronously with the arteries.

The brain differs from other organs, also, in that normally its volume is more influenced in a positive direction by the expiratory rise of venous pressure than by the inspiratory rise of general arterial pressure. Thus the rise of pressure in the thoracic veins which occurs with each expiratory act, causes a damming back of the venous blood in the sinuses and pial veins, resulting in a further increase in the volume of the brain and in the intra-cranial pressure. The reverse takes place in inspiration.

It has been ascertained experimentally that the intra-cranial pressure may vary considerably and consciousness still be preserved. Hill found it to be 40 to 50 mm. of Hg. in the convulsions of strychnin poisoning and a little less than zero in a patient standing erect.

The Regulation of the Volume of Blood Entering the Brain.—It is generally believed that the cerebral vessels are not provided with vaso-motor nerves. Every attempt to prove their existence either by physiologic or histologic methods has thus far failed of convincing proof. In the absence of vaso-motor nerves, the regulation of the circulation in the brain must necessarily be dependent on changes affecting the arterial and venous pressures in other regions of the body.

The most effective factor in increasing or decreasing the blood-supply to the brain resides in the power of the vaso-motor center to cause a contraction or dilatation of the cutaneous and splanchnic vessels. Thus if the vaso-motor center declines in its tonus from any cause whatever, there is a relaxation of the blood-vessels in one or both of these regions, an increase in the volume of the blood flowing into them, and in consequence, a decrease in the volume of the blood flowing through the brain. If on the contrary the vaso-motor center is increased in its tonus, the reverse conditions prevail in the cutaneous and splanchnic vessels and the quantity of blood flowing into the brain is increased. Thus in an indirect way the vaso-motor center, by bringing about a rise or a fall in the general arterial pressure, regulates the blood-supply to the brain, and controls its amount in accordance with its needs.

Brain Activity.—Brain activity is characterized by an active consciousness, the development of sensations, ideas, feelings, and the exercise of volitional power (which manifests in muscle movement) and is the result of a physiologic condition of the body at large. For the manifestation of brain activity it is essential that the irritability of the brain cells and more especially of those composing in large measure the cerebral cortex be maintained at a normal physiologic level, so that they may respond in the manner peculiar to them to the action of nerve impulses transmitted through afferent nerves from all regions of the body. Here as elsewhere throughout the body, the irritability depends on, and is maintained by, the presence of blood flowing into and out of the brain in varying quantity from moment to moment, with a given velocity and under a definite pressure. So long as these conditions are maintained in the strictly physiologic condition, so long will the brain respond to stimuli by the development of sensations. The avenues through which nerve impulses pass to the cortical cells are those beginning in the special and general sense organs of the body in contact with the external world, viz.: the eyes, ears, nose, tongue, and skin. The maintenance of these structures in a strictly physiologic condition is also one of the essential conditions for brain activity.

Judging from the changes in the character and composition of the blood which occur during its passage through the brain capillaries, there is coincidently with brain activity an active metabolism, which eventuates, at the end of a variable number of hours, in the decline of the irritability, a reduction of functional activity, and the establishment of the condition of fatigue. The irritability of the sense organs, especially of the eyes and ears, in all probability declines in a similar manner. These structures pass into the condition of fatigue and become less responsive to external stimuli. The results of all these conditions is a less active stimulation of the brain cells, which in connection with other factors predisposes to—

Brain Repose or Sleep.—Brain repose or sleep is characterized by a greater or less degree of unconsciousness, the non-development of sensations, ideas, feelings and volitional acts, and is the result of a diminution in the physiologic activities of the body at large and more especially of the brain, sense organs, and spinal cord. Coincident with the cessation of brain activity and the onset of sleep, there is a diminution in the rate and force of the heart-beat, and in the frequency and depth of the respiratory movements, and a relaxation of the skeletal muscles, especially those employed in voluntary movements.

The sense-organs are in part protected from the action of external stimuli. The eyeball is so turned that its anterior pole is directed far upward under the eyelid, while the pupil is markedly diminished in size, and in consequence the entrance of light largely prevented. The ear is protected against the reception of sounds of ordinary pitch by an increased tension of the tympanic membrane. The nose and mouth are less responsive to various stimuli because of the dryness of their mucous membranes from diminished secretion. The skin appears to be less sensitive to mechanic pressure and other forms of stimulation.

In addition to the foregoing phenomena, experimental investigations have shown that there is a shunting of a portion of the blood-stream from the brain to other regions of the body, especially to the skin and perhaps to the abdominal viscera as well, whereby it becomes incapable of functionating physiologically. The fact that the brain receives a lessened quantity of blood during sleep has been shown by trephining the skull and inserting in the orifice a glass plate through which the circulatory conditions of the brain can be observed. In the waking condition the blood-vessels on the surface of the brain are prominent, and turgid with blood and the whole organ completely fills the cranial cavity, indicating that the blood-vessels in the interior of the brain are in a similar condition. With the onset of sleep the larger blood-vessels begin to diminish in size, the smaller vessels disappear from view, the brain tissues become pale and the volume of the brain shrinks. During the continuance of deep sleep, this anemic condition persists. As the period of sleep approaches its termination, the smaller blood-vessels again fill with blood, the surface of the brain flushes, and in a very short time the former circulatory conditions return, the volume of the brain increases and the waking state is reëstablished.

The fact that the skin receives an increased volume of blood during sleep, has been shown by inserting an arm or leg in a plethysmograph by which means a record of any change in volume can be obtained. Howell thus succeeded in obtaining graphic records in the variations of the volume of the arm during sleep. These records disclosed the fact that with the onset of sleep the volume of the arm gradually increased in size until it attained a maximum which was from one to two hours after the beginning of sleep. After this period the volume remains practically the same for several hours, diminishing as the intensity of sleep diminishes and the waking state is approached. Just previous to the return of consciousness there is a rapid diminution in the volume of the arm. If it be accepted that the enlargement of the cutaneous vessels is followed by a diminution in size of the cerebral vessels, it follows that the former condition stands to the latter in the relation of cause and effect, whereby a portion of the blood is diverted from the brain to the skin. It also naturally follows that the withdrawal of the blood from the brain to the skin and possibly other regions as well, is the fundamental condition for brain repose.

The Intensity of Sleep.—Observations of individuals during sleep show that the intensity or the depth of sleep varies from hour to hour. Attempts have been made to estimate the intensity by measuring the loudness of a sound caused in several ways that is necessary to awaken the sleeper. Accepting this criterion it may be stated from the results of many experiments, that sleep increases in intensity or depth and reaches its maximum between the first and second hours, after which it rapidly decreases until the end of the third hour, when consciousness is so nearly restored, that but a very slight stimulus is required to awaken the sleeper. It is during the latter period when the brain is reviving that dreams arise, the elements of which are formed of previous sensations.

The Causes of Sleep.—Different theories have been proposed to account for the causes of sleep, none of which have been wholly satisfactory. From all the facts which have been presented it would appear that one cause is a decline in the irritability of the nerve-cells of the brain and associated sense-organs, and the development of fatigue conditions, the result of prolonged activity.

A second cause is the withdrawal of a large portion of the blood from the brain, on the presence of which, here as elsewhere, normal activity depends. As to whether the diminished activity of the brain is the cause of, or the result of the withdrawal of the blood there has been much difference of opinion. Howell has offered a plausible explanation for the withdrawal of the blood from the brain to the cutaneous vessels, based on the activity of the vasomotor center. He assumes that for a variable number of hours, corresponding to the usual waking state, this center possesses a certain average tonus, due in all probability to reflex influences, by virtue of which it maintains a certain average contraction of the cutaneous vessels. But at the end of this period it too becomes fatigued, declines in irritability, becomes less responsive to reflex influences, and hence loses its control over the vessels. As a result they dilate and thus reduce the amount of blood flowing to the brain to a level insufficient to maintain its activity, after which sleep supervenes. During sleep the irritability and tonus of the center are restored, when its control of the blood-vessels is regained. Unless the brain in its functional activities differs from all other organs of the body, it may be inferred that cessation of activity or repose is the result partly of fatigue and partly of a diminution of the blood-supply.

CHAPTER XXIV

THE CEREBELLUM

The cerebellum is situated in the inferior fossæ of the occipital bone beneath the posterior lobes of the cerebrum, from which it is separated by the tentorium cerebelli, a semilunar fold of the dura mater. It is partially divided into hemispheres by a longitudinal fissure, more apparent on the inferior surface, though united by a central lobe, the vermiform process. Each hemisphere is connected with the cerebrum, the pons, medulla, and spinal cord by three bundles of nerve-fibers known respectively as the *superior*, *middle*, and *inferior peduncles*. The surface of the cerebellum presents a series of lobes and fissures of which the former have received more or less fanciful names. A section of the cerebellum shows that it is composed of gray matter externally and white matter internally. The general appearance presented on section is shown in Fig. 255.

Structure of the Gray Matter.—The gray matter consists mainly of nerve-cells of varying size and shape, which are arranged in two layers: viz., an outer or molecular and an inner or granular.

The molecular layer consists of stellate and multipolar cells of small size, from which dendrites and axons pass horizontally and vertically. The granular layer consists, as its name implies, of granular-shaped cells and large stellate cells. These cells are characterized by the possession of dendrites and axons, the course and relation of which have not been clearly determined.

The inner border of the molecular layer presents a series of large cells originally described by Purkinje and known by his name. From the outer end of the cell-body one or more dendrities emerge which soon divide and subdivide into a number of branches which pass toward the cerebellar surface. The general arrangement of these dendrities gives to the entire cell a tree-like appearance (Fig. 256). From the inner end of the cell an axon emerges which passes centrally into the white matter.

Structure of the White Matter.—The white matter consists of nerve-fibers which are arranged in association and projection systems.

The Association System.—The fibers which compose this system are of variable lengths and unite adjacent as well as distant regions of the cerebellar cortex. They doubtless associate them both anatomically and physiologically.

The Projection System.—The fibers composing this system connect the cerebellar cortex with certain structures in the cerebrum, pons, medulla, and spinal cord. They may be divided into efferent and afferent systems.

The *efferent* fibers have their origin in the cells of Purkinje and the dentate nucleus. Some of these fibers emerge from the cerebellum in the superior peduncles through which they pass toward and beneath the corpora quadrigemina to terminate around the cells of the red nucleus. As they approach this nucleus some of the fibers cross the median line and decussate with those coming from the opposite side, while others pursue a straight direction, terminating on the same side. Through the intervention of fibers which arise in the red nucleus and ascend to the cerebral cortex, the hemisphere is thus connected with both sides of the cerebellum, though chiefly with the opposite side.

Efferent fibers also leave the cerebellum by the middle peduncle and pass directly to the *nucleus pontis*, around the cells of which their terminals arborize. Efferent fibers also descend the inferior peduncles and constitute the tract known as the Löwenthal and Marchi tract, situated in the antero-lateral region of the spinal cord in its upper part.

The *afferent* fibers come from a variety of sources. Those found in the superior peduncles come from the red nucleus; those in the middle peduncles from the nucleus pontis of the opposite side, having crossed or decussated at the raphé near the anterior surface of the pons; those contained in the inferior peduncles are the most abundant and important, and are represented by (1) the direct cerebellar tract, which terminates in the superior vermis after decussation; (2) the anterior and posterior arcuate fibers, the former coming from the gracile and cuneate nuclei of the opposite side, the latter from the same side, which also pass to the superior vermis; (3) the acoustico-cerebellar tract, composed of fibers which are the axons of the sensory end-nuclei (Deiters) of the vestibular portion of the auditory nerve. It is probable that all these fibers decussate prior to their final termination.

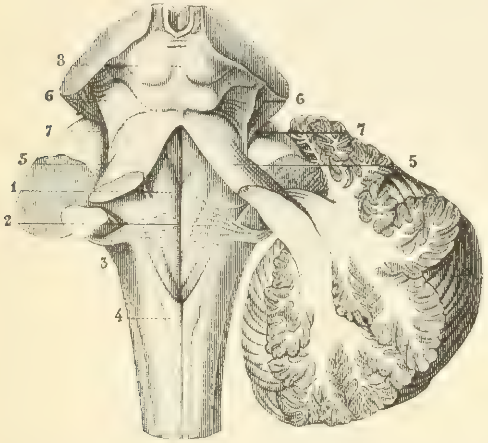

Fig. 255.—View of Cerebellum in Section and of Fourth Ventricle, with the Neighboring Parts.—(*From Sappey.*) 1. Median groove fourth ventricle, ending below in the calamus scriptorius, with the longitudinal eminences formed by the fasciculi teretes, one on each side. 2. The same groove, at the place where the white streaks of the auditory nerve emerge from it to cross the floor of the ventricle. 3. Inferior peduncle of the cerebellum, formed by the restiform body. 4. Posterior pyramid; above this is the calamus scriptorius. 5, 5. Superior peduncle of cerebellum, or processus e cerebello ad testes. 6, 6. Fillet to the side of the crura cerebri. 7, 7. Lateral grooves of the crura cerebri. 8. Corpora quadrigemina.—(*After Hirschfeld and Leveille.*)

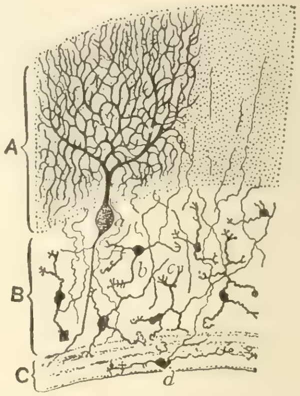

Fig. 256.—Section of Cerebellar Cortex. A. Outer or molecular layer. B. Inner or granular layer. C. White matter. *a.* Cell of Purkinje. *b.* Small cells of inner layer. *c.* Dendrites of these cells. *d.* A similar cell lying in the white matter.—(*Stirling.*)

The cerebellum through this system of efferent and afferent fibers is brought into relation with many different regions of the cerebrum, pons, medulla, and spinal cord. Each half of the cerebellum is connected with the foregoing structures of the same side, and of the opposite side.

THE FUNCTIONS OF THE CEREBELLUM.

From the observations of the results of experimental lesions, from the analysis of clinico-pathologic facts, and from the comparative anatomic development in different animals, the deduction has been drawn that the cerebellum coördinates and harmonizes the action of those muscles the activities of which are necessary to the maintenance of body equilibrium both during station and progression.

By *equilibrium* of the body is understood a condition which may be maintained for a variable length of time without displacement, and is possible only so long as a vertical line passing through the center of gravity falls within the base of support. The support offered by the earth to the feet neutralizes and counteracts the force of gravity. In standing, when the body is in the erect or military position, the arms by the side, the center of gravity lies between the sacrum and the last lumbar vertebra, and the line of gravity falls between the feet and within the base of support. The entire skeleton for the time being is rendered fixed and rigid at all its joints by the combined action of the muscles connected with it. That this position may be maintained all the different groups of antagonistic but coöperative muscles must be accurately coördinated in their actions. Any failure in this respect is at once attended by a disturbance of the equilibrium and displacement.

In progression, walking, running, dancing, etc., the body is translated from point to point by the alternate action of the legs. Whether the direction of the translation be rectilinear or curvilinear, as the legs change their position from moment to moment, the center of gravity also changes, and at once the equilibrium is menaced. If it is to be maintained and displacement prevented there must be a prompt readjustment in the relation of all parts of the body so that the line of gravity falls again within the base of support. The more complicated the moments of progression, or the narrower the base of support, the greater is the danger to the equilibrium, and hence the necessity for rapid and compensatory changes in coördinated muscle activity. All movements of this character, in man at least, are primarily volitional and require for their performance the constant exercise of the attention. With frequent repetition they gradually come to be performed independently of consciousness and fall into the category of secondary or acquired reflexes.

Though coördinating power is exhibited by the spinal cord, medulla, and basal ganglia, it is only in the cerebellum that this power attains its highest development and differentiation. To it is assigned the power of selecting and grouping muscles, not in any restricted part, but in all parts of the body, and coördinating their actions in such a manner as to preserve the equilibrium.

The Results of Experimental Lesions.—If the cerebellum in its totality coördinates and harmonizes the action of the muscles on the opposite sides of the body, any derangement of its structure or its connections with the cord, medulla, pons, or basal ganglia should at once be followed by incoördination of muscles and a want of harmony in their action. Experimental lesions of the cerebellum are attended by such results. The phenomena observed are many and complex. They differ in extent and character in different animals and in accordance with the extent and location of the lesion, though the note of incoördination runs through them all.

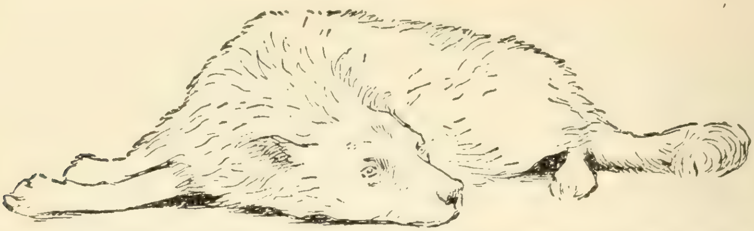

Fig. 257.—Attitude Assumed After Destruction of the Left Half of the Cerebellum.—(*Morat and Doyon, after Thomas.*)

Removal of one lateral half of the cerebellum in the dog is followed by an inability to maintain the equilibrium necessary to the erect position. On attempting to stand, the animal at once falls toward the side of the lesion, the muscles of which at the same time contract and give to the body a distinctly curved condition (Fig. 257). The anterior limbs are extended to the opposite side. On making efforts to regain the standing position, the animal may roll over around the long axis of its body. Conjugate deviation of the eyes is frequently observed as well as nystagmus.

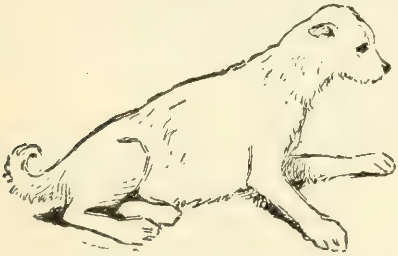

Fig. 258.—Attitude in Repose after the Complete Removal of the Cerebellum but during the Period of Restoration of Function.—(*Morat and Doyon, after Thomas.*)

After a few days the symptoms partially subside and the animal acquires the power of sitting on the abdomen when the anterior limbs are widely extended (Fig. 258). As the days go by the improvement continues, and the animal recovers the power of walking, though each step is attended with tremor and oscillations of the body. Any change in the center of gravity such as results when one leg is lifted may result in a fall toward the side of the lesion, owing to an inability to promptly bring about the necessary compensatory muscle actions. With time the animal continues to improve in its power of adjustment, though it never completely recovers it. Movements of progression are apt to be characterized by stiffness and accompanied by tremor suggestive of volitional efforts.

Total removal of the cerebellum is followed by a different train of symptoms. The extensor muscles apparently preponderate in their action, for the limbs are extended and abducted, the head and neck are retracted, and opisthotonos is established. In time these effects also partially subside, though all attempts at walking are permanently accompanied by tremor and oscillations. The characteristic effect which follows section of the peduncles is again incoördination, manifesting itself in deviation of the head, eyes, inability to walk, tremor on exertion, etc. The effects vary, however, according to the peduncle divided. Section of the middle peduncle gives rise to the most pronounced effects. The head and the anterior part of the body are at once drawn toward the pelvis on the side of the section. A voluntary effort on the part of the animal causes it to lose all control of its muscles and the body is rotated around its longitudinal axis from 40 to 60 times a minute before it comes to rest. According as the lesion is made from behind or before, the rotation is from or to the side of the section. In time these symptoms subside, though the animal never completely recovers.

The partial recovery of the power of coördination, observed after removal of a portion or the whole of the cerebellum, indicates that the centers in the cord, medulla, pons, and cerebrum endowed with corresponding though less developed power, develop compensatory activity and acquire to some extent the capabilities of the cerebellum itself (Fig. 259).

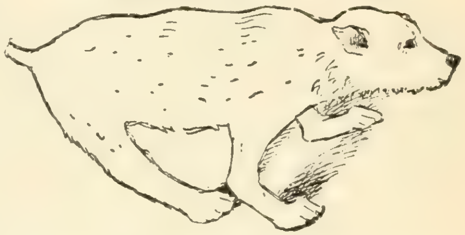

Fig. 259.—Progression after Destruction of the Vermis.—(*Morat and Doyon, after Thomas.*)

Clinico-pathologic facts partly corroborate the results of physiologic investigations. In various forms of uncomplicated cerebellar disease, vertigo, tremor on making voluntary efforts, difficulty in maintaining the erect position, unsteadiness in walking, opisthotonos, pleurothotonos, are among the symptoms generally observed.

Comparative anatomic investigations reveal a remarkable correspondence between the development of the cerebellum and the complexity of the movements exhibited by animals. In those animals whose movements are complex and require for their performance the coöperation of many groups of muscles the cerebellum attains a much greater development in reference to the rest of the brain than in animals whose movements are relatively simple in character. This relative increase in the development of the cerebellum is found in many animals, as the kangaroo, the shark, the swallow, and the predaceous birds generally.

The Coördinating Mechanism.—Though it is not known how the cerebellum selects and coördinates groups of muscles for the performance of any complex movement, it is known that its activity is largely reflex in origin and excited by impulses which come to it from peripheral organs. In this as in other forms of reflex activity the mechanism involves (1) afferent nerves, *e.g.*, cutaneous, muscle, optic, and vestibular, and their related end-organs, tactile corpuscles, muscle spindles, retina, and semicircular canals, all indirectly connected with (2) the cerebellar centers; (3) efferent nerves indirectly connected with (4) the general musculature of the body. Both station and progression are directly dependent on the development and transmission of afferent impulses from the previously mentioned peripheral sense-organs to the cerebellum. Tactile, muscle, visual, and labyrinthine impressions and sensations not only coöperate in the development and organization of the motor adjustments necessary to the maintenance of the equilibrium and locomotive coördination, but even after their organization they are necessary to the excitation of cerebellar activity. The manner in which they lead to the development of this capability on the part of the cerebellum is conjectural. Their ever-present influence is shown by the effects which follow their removal, as the following facts indicate.

The prevention of the development of *tactile* impulses by freezing or anesthetizing the soles of the feet, and the blocking of normally developed impulses through destruction of afferent pathways in diseases of the spinal cord lead at once to make impairment in the coördinating power. The removal of the skin from the hind legs of the frog, previously deprived of its cerebrum, destroys its coördinating power, which it would otherwise possess in a high degree.

The blocking, in consequence of destructive lesions of the spinal cord, of the impulses, which come from the *muscles*, *tendons*, etc., and which inform us of the activity and the degree of activity of our muscles, the location of limbs, the amount of effort necessary to produce a given movement, etc., also gives rise to much incoördination. A blocking of both tactile and muscle impulses frequently exists in degeneration or sclerosis of the posterior columns of the spinal cord. The coördinating power is so much impaired in this disease that the patient is unable to maintain, without strained effort, the erect position and especially if the directive power of the eyes be removed by closure of the lids. Walking becomes extremely difficult; the gait is irregular and jerky, and equilibrium is maintained only by keeping the eyes fixed on the ground in front and by artificially increasing the basis of support by the use of canes.

An interference with the development of the customary *visual* impressions which in a measure maintain the sense of relation of the individual to surrounding objects also gives rise to equilibratory disturbances. A rapid change in the relation of the individual to surrounding objects or the reverse; a change in the direction of one optic axis from the use of a prism or from paralysis of an eye muscle; the destruction of an eye—these and similar conditions frequently give rise to such marked disturbances of the equilibratory power that displacement is difficult to prevent.

An interference with the development of the so-called *labyrinthine* impressions by destruction of the semicircular canals gives rise to the most remarkable disturbances in this respect. Section of one horizontal canal[1] in the pigeon is followed by oscillations of the head in a horizontal plane around a vertical axis. Bilateral section so increases these oscillations that the pigeon is unable to maintain equilibrium and forced to fall and turn continuously around the vertical axis. Bilateral section of the posterior vertical canals gives rise to oscillations around a horizontal axis which frequently become so exaggerated as to eventuate in the turning of backward somersaults, head over heels. Similar phenomena follow division of the superior vertical canals.

Bilateral destruction of both sets of canals is attended by extraordinary disturbances in the equilibrium. From the moment of the operation the animal, the pigeon, loses all control of its motor mechanisms. It can neither maintain a fixed attitude nor execute orderly movements of progression; its activity, continuous and uncontrollable, is characterized by spinning around a vertical axis, turning somersaults, dashing itself against surrounding objects until life is endangered. If the animal be protected from injury, these disturbances gradually subside, and in the course of a few months the equilibratory power is so far regained that standing and walking at least become possible. In this condition, however, the coördinating power is directly dependent on visual impulses, for with the closure of the eyes all the previous motor disturbances at once recur. These and similar facts indicate that the semicircular canals are the peripheral sense-organs from which come the nerve impulses most essential to the excitation of the cerebellar coördinative centers in their control of equilibrium and of progression.

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[1] The physiologic anatomy of the semicircular canals is described in the chapter devoted to the ear, to which the reader is referred.

The cerebellum may therefore be regarded as the essential, most highly differentiated portion of the coördinating mechanism concerned in the maintenance of equilibrium, during both station and progression. The manner in which the cerebellum accomplishes this result is unknown, though it is certain, from the foregoing facts, that its special mode of activity is dependent on the excitatory action of nerve impulses transmitted from a variety of peripheral sense-organs.

CHAPTER XXV

THE ENCEPHALIC OR CRANIAL NERVES

The nerve-trunks which serve as channels of communication between the encephalon and the structures of the head, the face, and in part the organs of the thorax and abdomen, pass through foramina in the walls of the cranium, and for this reason are termed cranial nerves.

According to the classification now generally adopted, there are twelve cranial nerves on either side of the median line, which, enumerated from before backward, are as follows (Fig. 260):

The First or Olfactory.
The Second or Optic.
The Third or Oculo-motor.
The Fourth or Trochlear.
The Fifth or Trigeminal.
The Sixth or Abducent.
The Seventh or Facial.
The Eighth or Acoustic.
The Ninth or Glosso-pharyngeal.
The Tenth or Pneumogastric or Vagus.
The Eleventh or Spinal Accessory.
The Twelfth or Hypoglossal.

The cranial nerves may be classified physiologically in accordance with their functional manifestations into three groups, viz.:

1. The Nerves of Special Sense: *e.g.*, Olfactory, Optic, Acoustic, Gustatory (Glosso-pharyngeal and Chorda tympani).
2. The Nerves of General Sensibility: *e.g.*, Large root of the Trigeminal, Glosso-pharyngeal, and Pneumogastric.
3. The Nerves of Motion: *e.g.*, Oculo-motor, Trochlear, the small root of the Trigeminal, Abducent, Facial, Spinal Accessory, and Hypoglossal.

Though this classification in the main holds true, it must be borne in mind that modern investigations have demonstrated that the glosso-pharyngeal and pneumogastric nerves contain even at their junction with the medulla oblongata a number of efferent or motor fibers, and to this extent are mixed nerves.

The Origins of the Cranial Nerves.—In accordance with modern views as to the origins of nerves in general, it may be stated that—

The *nerves of special sense* have their origin respectively in the neuro-epithelial cells in the mucous membrane of the olfactory region of the nose, in the ganglion cells of the retina, in the cells of the spiral ganglion of the cochlea and the ganglion of Scarpa, and in the cells of the petrous and jugular ganglia. From the cells of these ganglia dendrites pass peripherally to become associated with specialized end-organs, while axons pass centrally in well-defined bundles to become related by means of their end-tufts with primary basal ganglia.

The *nerves of general sensibility* have their origin in the ganglia on their trunks, and in this respect resemble the spinal nerves. From the ganglion cell there emerges a short axon process which soon divides into a central and a peripheral branch. The former passes toward and into the gray matter located beneath the floor of the fourth ventricle, where its end-tufts arborize about nerve-cells. The latter (the peripheral branch) passes toward the general periphery to be distributed to skin and mucous membranes.

The *nerves of motion* have their origin in the nerve-cells in the gray matter beneath the aqueduct of Sylvius and beneath the floor of the fourth ventricle. The axons emerging from these cells course peripherally to be distributed to skeletal muscles. In some of the motor nerves, and in some sensor nerves as well, there are to be found efferent fibers of smaller size which have a similar origin and which become related through the intervention of sympathetic ganglia (peripheral neurons) with visceral and vascular muscles and glands. These nerves have been termed autonomic nerves.

The Cortical Connections of the Cranial Nerves.—Each of these three groups of cranial nerves has special connections with the cerebral cortex.

The *nerves of special sense* for the most part terminate in primary basal ganglia, around the cells of which their central end-tufts arborize. From these cells axons arise which pass upward and directly or indirectly come into physiologic relation with sensor nerve-cells in the cerebral cortex.

The *nerves of general sensibility* terminate in the gray matter beneath the floor of the fourth ventricle, around the nerve-cells of which their end-tufts arborize. These groups of nerve-cells are known as sensor end-nuclei. Though once regarded as the centers of origin of the sensor nerves, they are now regarded as the centers of origin of axons which pass upward to the cortex of the cerebrum, where they also come into physiologic relation with sensor nerve-cells.

The axons in both of these classes of nerves thus originate in the cells of the central nerve system and continue upward to the cerebrum, the primary afferent path.

The *motor nerves* which have their origin in the cells of the gray matter beneath the aqueduct of Sylvius and beneath the floor of the fourth ventricle are in physiologic relation with nerve-cells in the motor region of the cortex through descending axons contained in the pyramidal tract, the end-tufts of which arborize around the nerve-cells. The efferent path beginning in the cerebral cortex is thus continued by the motor nerves to the general periphery.

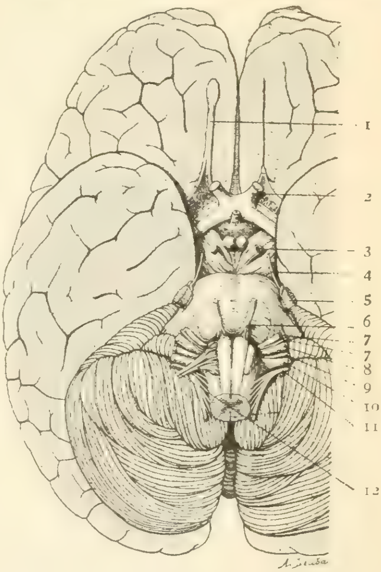

Fig. 260.—Superficial Origin of the Cranial Nerves from the Base of the Encephalon. 1. Olfactory. 2. Optic. 3. Motor oculi. 4. Trochlear. 5. Trigeminal. 6. Abducent 7. Facial. 7'. Nerve of Wrisberg. 8. Acoustic. 9. Glosso-pharyngeal. 10. Pneumogastric. 11. Spinal accessory. 12. Hypoglossal.—(*Morat and Doyon.*)

The three groups of nerves, those of special sense, of general sensibility, and the motor nerves, are neurons of the first order; the nerve-cells and fibers which constitute the cerebral connections are neurons of the second order. It is probable that the sensor cells in the cerebral cortex are neurons of a third order.

THE FIRST NERVE. THE OLFACTORY

The first cranial nerve, the olfactory, is situated in the upper third of the nasal fossa, in the *regio olfactoria.* It consists of from 20 to 30 branches, the fibers of which are non-medullated.

Origin.—The olfactory nerve is composed of centrally coursing axons which have their origin in the central ends of bipolar, rod-shaped, or spindle-shaped nerve-cells interspersed among the epithelial cells covering the mucous membrane in the regio olfactoria; the peripheral ends of these cells give off a number of dendrites which are spread out to form a delicate feltwork over the surface of the mucous membrane. From their origin the axons gradually converge to form bundles which ascend to the cribriform plate of the ethmoid bone, through the foramina of which they pass to become related by their end-tufts with structures in the gray matter of the olfactory bulb (Fig. 261).

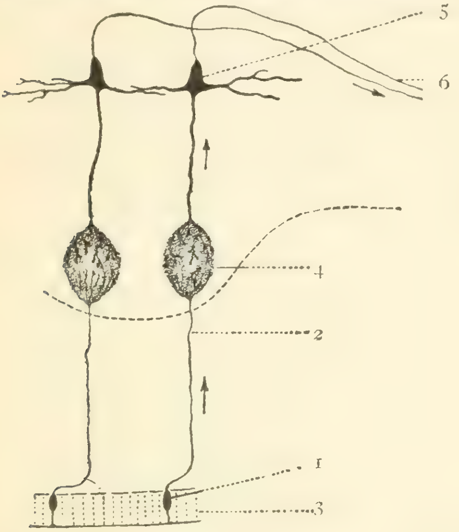

FIG. 261.—THE RELATION OF THE OLFACTORY NERVES TO THE OLFACTORY TRACT. 1. Olfactory nerve-cell. 2. Axon process. 3. Epithelial cells. 4. Glomerulus. 5. Mitral cells. 6. Centrally coursing axons of the olfactory tract.—(*Morat and Doyon.*)

Cortical Connections.—The olfactory bulb and olfactory tract, formerly called the olfactory nerve, are portions of the cerebrum (the olfactory lobe) which arise embryologically by a protrusion of the walls of the cerebral cavity. The bulb is oval-shaped and consists of both gray and white matter. It rests on the cribriform plate of the ethmoid bone and is embraced by the olfactory nerves. As seen on sagittal section, there is just beneath the surface a layer of large pyramidal and spindle-shaped cells (termed also mitral cells), each provided with an apical and two lateral dendrites. The apical dendrite passes toward the surface and ends in a brush- or basket-like expansion which interlaces with the end-tufts of the olfactory nerves, forming what are known as the olfactory glomerules. The lateral dendrites end free.

The axons of the pyramidal cells pass toward the center of the bulb and bend at right angles, after which they pursue a horizontal direction toward and into the *olfactory tract.* This tract is about five centimeters in length, prismatic in shape on cross-section and divisible into a *ventral* and a *dorsal* portion. It emerges from the posterior extremity of the bulb, passes backward to the posterior part of the anterior lobe, where it divides into three roots: viz., a lateral or external, a mesial or internal, a middle or dorsal. The fibers of the lateral and mesial roots are derived almost exclusively from the *ventral* portion of the tract, the fibers of which come from the mitral cells in the bulb. The lateral root-fibers pass outward into the fossa of Sylvius and come into relation with nerve-cells in the inferior extremity of the gyrus hippocampus and the gyrus uncinatus. The mesial fibers pass inward and come into relation with nerve-cells in the pre-callosal part at least of the gyrus fornicatus. The fibers thus far considered are undoubtedly true olfactory fibers, pursuing a centripetal direction, carrying nerve impulses from the olfactory cells to the cerebrum (Fig. 262).

Histologic and embryologic methods of research have shown that some of the fibers in the olfactory tract are centrifugal in function. They originate in the olfactory cortical areas, pass toward the periphery as far as the anterior commissure, where they cross to become the dorsal root, enter the olfactory tract, and finally terminate in the bulb. This tract serves to connect the cortex with the bulb of the opposite side, and carries impulses from the cortex to the bulb. The two opposite cerebral olfactory areas are also united by commissural fibers which decussate at the anterior commissure.

Function.—The function of the olfactory system in its entirety is the transmission of nerve impulses from its origin in the olfactory region of the nose to the cerebral cortex, where they evoke sensations of odor. The stimulus to its excitation is the impact and chemic action of gaseous or volatile organic matter on the dendrites of the olfactory cells. The sensitiveness of the olfactory end-organ to the action of many substances is remarkable, responding, for example, to the $\frac{1}{1200000}$ of a gram of oil of roses and to the $\frac{1}{2760000}$ of a gram of mercaptan.

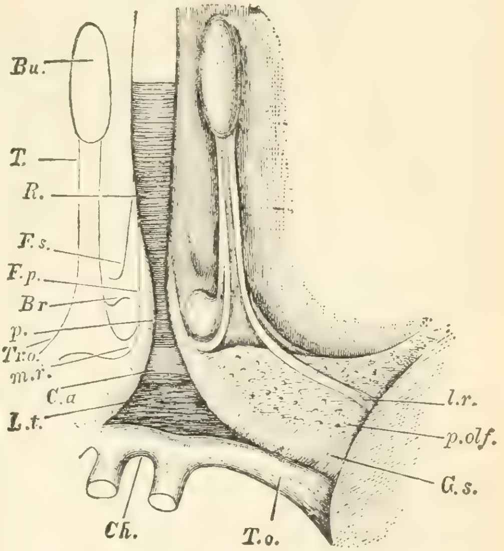

FIG. 262.—OLFACTORY LOBE OF THE HUMAN BRAIN. —*Bu.* Olfactory bulb. *T.* Tract. *Tr.o.* Trigone. *R.* Rostrum of corpus callosum. *p.* Peduncle of corpus callosum, passing into *G. s.*, gyrus subcallosus (diagonal tract, Broca). *Br.* Broca's area. *F.p.* Fissura prima. *F.s.* Fissura serotina. *C.a.* Position of anterior commissure. *L.t.* Lamina terminalis. *Ch.* Optic chiasma. *T.o.* Optic tract. *p. olf.* Posterior olfactory lobule (or anterior perforated space). *m.r.* Mesial root. *l.r.* Lateral root of tract.—(*His.*)—*After Quain.*)

Division or destruction of the olfactory path at any point is followed by an abolition of the sense of smell on the corresponding side. Destructive lesions of the hippocampal and uncinate gyri are followed by similar results.

THE SECOND NERVE. THE OPTIC

The second cranial nerve, the optic, consists of centrally coursing axons of neurons which connect the essential part of the organ of vision, the retina, with sensory end-nuclei or ganglia situated at the base of the cerebrum.

Origin.—The axons which constitute the optic nerve have their origin in the ganglion cells in the anterior part of the retina. Through their dendrites these cells are brought into relation posteriorly with successive layers of cells which collectively constitute the retina. Though the retina is said to consist of ten or eleven layers, it may be reduced practically to three, viz. (Fig. 263):

1. The layer of visual cells.
2. The layer of bipolar cells.
3. The layer of ganglionic cells.

The *visual cells* present peripherally modified dendrites, known as the rods and cones; centrally they give off an axon which after a short course terminates in an end-tuft. The *bipolar cells* also possess dendrites and an axon; the former interlace with the end-tufts of the visual cell axon, the latter with the dendrites of the ganglion cell. The retina may be regarded therefore as the peripheral end-organ in which the optic nerve originates. From their origin the axons turn backward, at the same time converging to form a distinct bundle which passes through the chorioid coat and sclera. After emerging from the eyeball the nerve-bundle (the optic nerve) passes backward as far as the sella turcica, traversing in its course the orbit cavity and the optic foramen. At the sella turcica there is a union and partial decussation in man and other mammals of the two nerves, forming the *optic chiasm.*[1]

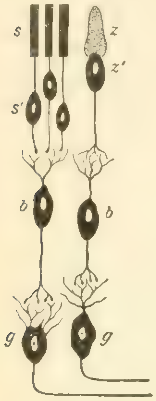

FIG. 263.—RETINAL CELLS. *s'*, *z'*. Visual cells with their peripheral terminations. *s*. Rods. *z*. Cones. *b*. Bipolar cells. *g*. Ganglion cells from which arise the axons of the optic nerve.

The Decussation of the Optic Nerves.—The extent to which the fibers from each eye decussate at the chiasm is a subject of dispute, but the results of various methods of research would seem to indicate that the fibers from the nasal third of the retina of the left eye cross in the chiasm, to unite with the fibers from the temporal two-thirds of the retina of the right eye. In a similar manner the fibers from the nasal third of the retina of the right eye cross in the chiasm, and unite with the fibers from the temporal two-thirds of the retina of the left eye (Fig. 264). Posterior to the chiasm the crossed and uncrossed fibers form the so-called optic tracts, which after winding around the crura cerebri enter the optic basal ganglia. Transection of the optic nerve shows that it is composed of an enormous number of non-medullated nerve-fibers, estimated by Salzer at from 450,000 to 800,000, enclosed in a sheath of the dura mater.

The visual fibers comprising the optic nerve may be physiologically divided into two clases, (*a*) those coming from the peripheral portion of the retina, and (*b*) those coming from that central area known as the macula lutea. The retinal fibers are by far the more abundant, and make up the major portion of the nerve; the macular fibers are less abundant. An examination of a cross-section of the optic nerve shows the presence of a wedge-shaped tract occupying the center of the nerve which is regarded as composed of the macular fibers. At the chiasm this bundle of fibers undergoes a partial decussation similar to that of the fibers coming from the more peripheral portions of the retina. In the left optic tract, therefore, fibers from at least four different regions are to be found: viz., the two-thirds of the temporal side of the left retina, the temporal half of the left macula, the nasal third of the right retina, and the nasal half of the right macula. Corresponding fibers are to be found in the right optic tract. As the optic tract passes around the crus cerebri it divides into a lateral or outer, and a mesial or inner bundle, which then terminate in **the optic basal ganglia.** The fibers of the lateral bundle are traceable into the lateral or external geniculate body (the pre-geniculum), the pulvinar of the optic thalamus, and the anterior quadrigeminal body (the pre-geminum). With the exception of the fibers passing to the anterior quadrigeminal body, these are in all probability the true visual fibers. The fibers of the mesial bundle are traceable into the internal geniculate body (the post-geniculum) and the posterior quadrigeminal body (the post-geminum). These fibers are not a part of the optic nerve proper, but commissural fibers associating the internal geniculate bodies of the two sides. (*Gudden's Commissure.*)

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[1] Though the foregoing is the usual method of stating the origin and course of the optic nerve, nevertheless morphologically the true optic nerve lies wholly within the retina and is composed of the visual cells there found. The remainder of the visual system from and including the ganglion cells of the retina to the optic basal ganglia, is the optic tract, there being no anatomic or physiologic distinction between the optic nerve so called and the *optic tract*. Both are outgrowths from the brain and hence possess properties which differentiate them from other cranial nerves.

Cortical Connections.—After entering the pulvinar and the lateral or external geniculate body the visual fibers terminate in end-tufts which arborize around nerve-cells. From these cells new axons arise which ascend through the posterior part of the internal capsule, at the same time curving backward to form the optic radiation of Gratiolet, and terminate finally around nerve-cells in the gray matter of the cuneus and in the gray matter bordering the calcarine fissure, both situated on the mesial aspect of the occipital lobe.

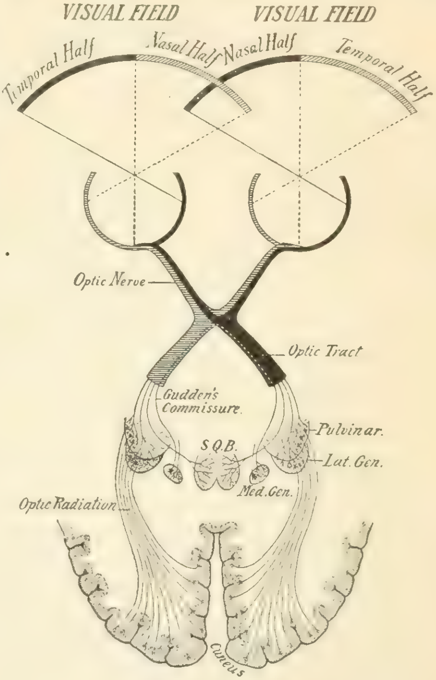

FIG. 264.—DIAGRAM ILLUSTRATING LEFT HOMONYMOUS LATERAL HEMIANOPSIA FROM A LESION OF THE RIGHT OPTIC TRACT OR THE RIGHT CUNEUS. THE SHADED LINES IN THE VISUAL FIELDS INDICATE THE DARKENED AREA.

Centrifugal Fibers of the Optic Nerve.—All the fibers previously alluded to have been afferent or centripetal in direction; but the optic nerve also contains efferent or centrifugal fibers which come from nerve-cells in the basal ganglia and ramify around special cells, the amacrine cells, in the retina. Their function is unknown. It has been suggested that they regulate the vascular supply to the retina. Centrifugally coursing fibers also connect the visual areas of the cortex with the superior quadrigeminal body.

Function.—The function of the optic nerve and tract is the transmission of nerve impulses from the retina to the cerebral cortex where they evoke the sensations of light and its different qualities—colors. The specific physiologic stimulus to the retinal visual cells is the impact of the undulations of the ether. In general it may be said that, at least for the same color, the intensity of the objective undulation or vibration determines the intensity of the sensation.

Owing to the partial decussation of the optic nerve-fibers at the chiasma, the impressions made on the temporal side of the retina are received by the cuneus of the same side, while the impressions made on the nasal side are received by the cuneus of the opposite side. Each eye is, therefore, associated with the cuneus of each cerebral hemisphere.

Pupillary Fibers.—The optic nerve also contains nerve-fibers somewhat larger in caliber than the usual visual fibers, which are supposed to form the afferent path for those nerve impulses which excite reflexly a contraction of the *sphincter pupillæ* muscle, thus varying the size of the pupil. These fibers, termed pupillary fibers, come from all portions of the retina but most abundantly from the posterior pole in and around the macula. The existence of these fibers is confirmed by pathologic findings. In a manner similar to that of the visual fibers they, too, undergo a decussation in the optic chiasm, so that in the optic tract there are pupillary fibers which come from the temporal side of the eye of the corresponding side, and fibers which come from the nasal side of the eye of the opposite side (Fig. 268, page 620). The central termination of these fibers is not positively known.

Hemiopia and Hemianopsia.—Division of the optic nerve between the eyeball and the optic chiasm is followed by complete blindness in the eye of the corresponding side. Owing to the partial decussation of the fibers in the chiasm, division of an *optic tract* is followed by a loss of sight in the *outer two-thirds* of the eye of the same side and in the inner third of the eye of the opposite side. To this loss of visual power in the retina the term *hemiopia* is given. In consequence of this loss of visual power in the retina there is a corresponding obscuration or total obliteration of nearly one-half of the visual field,[1] to which the term *hemianopsia* is given. If, for example, the *right optic tract* is divided there will be hemiopia in the outer two-thirds of the right eye and the inner third of the left eye, with *left lateral hemianopsia*, and as the portions of the retina which are affected are associated in vision the loss of the visual fields is spoken of as homonymous hemianopsia (Fig. 266). A destructive lesion of the cerebral visual area, the cuneus and the adjacent gray matter on the right side, is also followed by left lateral hemianopsia.[2]

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[1] The visual field comprises that portion of the external world from which, with the eyes stationary, rays of light pass to the retinæ and is the area included between the extremes of the visual lines entering the pupil. The center of the visual field is the area the rays of light from which are focalized on the fovea centralis. The visual field is somewhat irregular in outline by reason of the position of the eyeball in the orbit cavity, and the consequent interference with the entrance of light by the bridge of the nose, the cheek bones, and the eyebrows. The horizontal diameter of the visual field for the right eye is about 150°, of which 90° pertain to the temporal and 60° to the nasal portion. The vertical diameter is about 115°, of which 45° pertain to the superior and 70° to the inferior portion. By reason of the position of the eyes in the orbit cavity the two visual fields, viz.: that of the right and of the left eye, overlap to a variable extent in their nasal divisions.

[2] It should be borne in mind that in both instances the retina itself is unaffected. The impact of light generates, as usual, nerve impulses which proceed as far backward as the point of division or destruction. In consequence those portions of the cerebral cortex stimulation of which evokes the sensation of light remain unaffected and the individual does not become aware, through sensation, of the presence of a luminous body in the left side of the visual field.

The existence of a homonymous hemianopsia becomes evident when the individual is directed to focus the vision on an object placed directly in front and with its center in the median plane of the body, when if the lesion be on the right side, the left half of the object will be invisible. The reason for this will be apparent on reference to Fig. 265. All the light rays emanating from the left half of the object fall on the retina on the side of the injury, and hence there will be no sensation. If, however, the object be moved to the right without change in the position of the head, the entire object will be visible, as all the rays fall on the normal side. If, on the contrary, the object be moved to the left, it will be invisible for the opposite reason.

Hemianopsia may be the result of either destruction of the optic tract or of the cortical visual area. The seat of lesion in any given case is indicated by a peculiarity of the iris reflex pointed out by Wernicke, which will be referred to in connection with the consideration of the oculo-motor nerve.

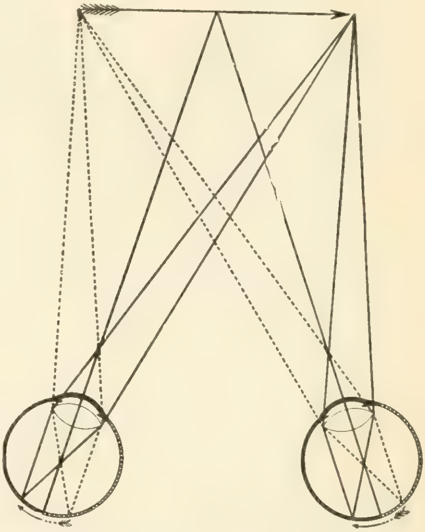

Fig. 265.—Diagram to Show the Existence of Hemianopsia. The lesion is supposed to be in the right optic tract.

THE THIRD NERVE. THE OCULO-MOTOR

The third cranial nerve, the oculomotor, consists of some 15,000 peripherally coursing nerve-fibers which serve to bring the nerve-cells from which they arise into relation with a large portion of the general musculature of the eye.

Origin.—The axons composing the third nerve arise from a series of seven or eight groups of nerve-cells, located in the gray matter beneath the floor of the aqueduct of Sylvius. From each of these groups or nuclei, bundles of axons emerge, which after a short course unite to form the common trunk. The large majority of the fibers in the nerve come directly from the nuclei of the same side; the remainder come from a group of cells on the opposite side of the median line. There is thus a partial decussation of its fibers (Fig. 266).

The different groups of cells, the nuclei of origin, are arranged in a serial manner. The anatomic arrangement of these nuclei would indicate that each nucleus is related to an individual member of the eye-group of muscles. Clinical observation and the investigation of the results of pathologic processes have not only shown that this is the case, but also succeeded in locating the position of the nucleus for any given muscle. Though there is some difference of opinion in regard to the exact location of one or two of the nuclei, the tabulation subjoined is approximately correct.

Enumerating them from before backward, the nuclei occur in the following order:

1. The sphincter pupillæ.
2. The tensor chorioideæ (the accommodation nucleus).

3. The convergence nucleus, a common nucleus for the *conjoint* action of the two internal recti muscles.
4. The superior rectus.
5. The inferior rectus.
6. The levator palpebræ.
7. The inferior oblique.

Cortical Connections.—The oculo-motor nuclei are in histologic and physiologic relation with the motor area of the cerebrum. Nerve-cells in the cortex give off axons which, entering the pyramidal tract, descend through the internal capsule, and the crus cerebri, from which they cross to the opposite side. The end-tufts arborize around the nuclei of the oculo-motor nerve with the exception of the nucleus for the iris sphincter.

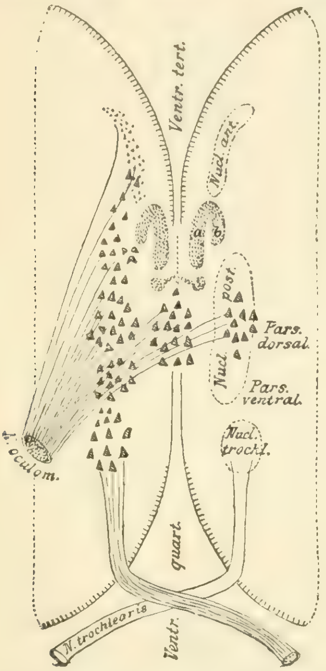

FIG. 266.—DIAGRAMMATIC VIEW OF THE SITUATION AND RELATION OF THE NUCLEI OF ORIGIN OF THE OCULO-MOTOR AND PATHETICUS (TROCHLEARIS) NERVES. The oculo-motor nuclei consist of an anterior nucleus, the Edinger-Westphal nucleus (*a* and *b*), and a posterior nucleus; the posterior nucleus has a dorsal, a ventral, and a mesial portion; the decussation of fibers from the dorsal portion of the posterior nucleus is also shown. The decussation of the fibers of the fourth nerve is also represented. —(*Edinger.*)

Distribution.—After their origin the axons converge to form a common trunk, which emerges from the base of the encephalon, on the inner side of the crus cerebri, in front of the pons Varolii. The nerve then passes forward through the sphenoid fissure into the orbit cavity, where it divides into a *superior* and an *inferior* branch. The former is distributed to the *superior rectus* and the *levator palpebræ* muscles; the latter is distributed to the *internal* and *inferior recti* and *inferior oblique* muscle (Fig. 267).

From the inferior branch a short bundle of fibers passes to the *ciliary* or *ophthalmic* ganglion, where they terminate, arborizing around the ganglion cells. These fibers are smaller in size than those constituting the bulk of the nerve and belong to the system known as the autonomic. These cells give origin to new axons, *the ciliary nerves*, which enter the eyeball, pass forward between the sclera and chorioid coat, and terminate in the *ciliary muscle* and the *sphincter* of the pupil. The ciliary nerves are not portions of the third nerve proper, but peripheral sympathetic neurons. As the ciliary ganglion receives filaments from the cavernous plexus of the sympathetic and filaments which become a part of the trigeminal nerve, it is probable that the ciliary nerves contain not only motor, but vaso-motor and sensor fibers as well.

Properties.—*Stimulation* of the nerve near its exit from the encephalon is followed by contraction of the muscles to which it is distributed with the following results, viz.:

1. Diminution in the size of the pupil.

2. Accommodation of the eye for near vision.
3. Elevation of the upper eyelid.
4. Internal deviation and rotation upward and inward of the anterior pole of the eye, combined with a small amount of torsion toward the mesial line, due to preponderating action of the internal rectus and inferior oblique muscles.

Division of the nerve either experimentally or as a result of compression from a pathologic cause is followed by a relaxation of the muscles, with the following effects, viz.:

1. Dilatation of the pupil, the iris responding neither to light nor to efforts of accommodation.
2. Loss of the accommodative power.
3. Falling of the upper eyelid (ptosis).
4. External deviation and rotation downward and outward of the anterior pole of the eyeball combined with a small amount of torsion toward the mesial line due to the unopposed action of external rectus and the superior oblique muscles.
5. Double vision or diplopia. The image of the eye of the paralyzed side is projected to the opposite side of the true image and to the upper part of the visual field. Owing to the slight mesial torsion the false image is inclined away from the true image.
6. Immobility and slight protrusion of the eyeball.

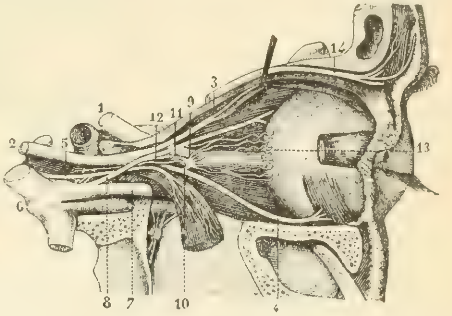

Fig. 267.—Intra-orbital Portion of the Third Nerve. 1. Optic nerve. 2. *Third nerve.* 3. *Superior branch.* 4. *Inferior branch.* 5. Abducens. 6. Trifacial. 7. Ophthalmic branch divided. 8. Nasal branch. 9. *Ciliary ganglion.* 10. *Motor branch* to this ganglion from the inferior branch of the third nerve. 11. Sensory fibers. 12. Sympathetic fibers. 13. *Ciliary nerves.*—(*Sappey.*)

Function.—The function of the third nerve is to transmit nerve impulses from the nuclei of origin to all the muscles of the eye except the external rectus and superior oblique and excite them to activity. The majority of the ocular movements, the power of accommodation, the variations in the size of the pupil in accordance with variations in the intensity of the light, the power of convergence of the visual axes, are all excited by the transmission of nerve impulses by the constituent fibers of the nerve from their related nuclei. This is made evident by the effects which follow stimulation and division of the nerve or lesions of the nuclei themselves.

The central nuclei can be excited to activity (1) by nerve impulses descending the motor tract, from the cerebral cortex, (2) by nerve impulses coming through various afferent nerves. This holds true more especially for the sphincter pupillæ nucleus.

The Iris Reflex or the Pupillary Reflex.—These are terms applied to the variations in the size of the pupil that follow variations in the intensity of the light. In the absence of light the pupil widely dilates, due largely to the relaxation of the *sphincter pupillæ* muscle and partly to a contraction of the radiating fibers of the iris, which collectively constitute the *dilatator pupillæ* muscle. With the entrance of light into the eye, the pupil diminishes in size, in consequence of the contraction of the *sphincter pupillæ* caused by a stimulation of the peripheral ends of the pupillary fibers of the retina, the degree of contraction depending within limits on the intensity of the light.

The action of the sphincter pupillæ muscle is, therefore, a reflex action and involves the usual mechanism, viz.: A receptive surface, the retina; afferent nerves, the pupillary fibers in the optic nerve; an emissive center, the sphincter nucleus of the motor oculi center; efferent nerves, including fibers in the trunk of the motor oculi and in the ciliary nerves; and a responsive organ, the muscle. (See Fig. 268). That this is the mechanism involved in this reflex, is shown by the fact that when any portion of it is destroyed, the reflex contractions of the sphincter are impaired or abolished.

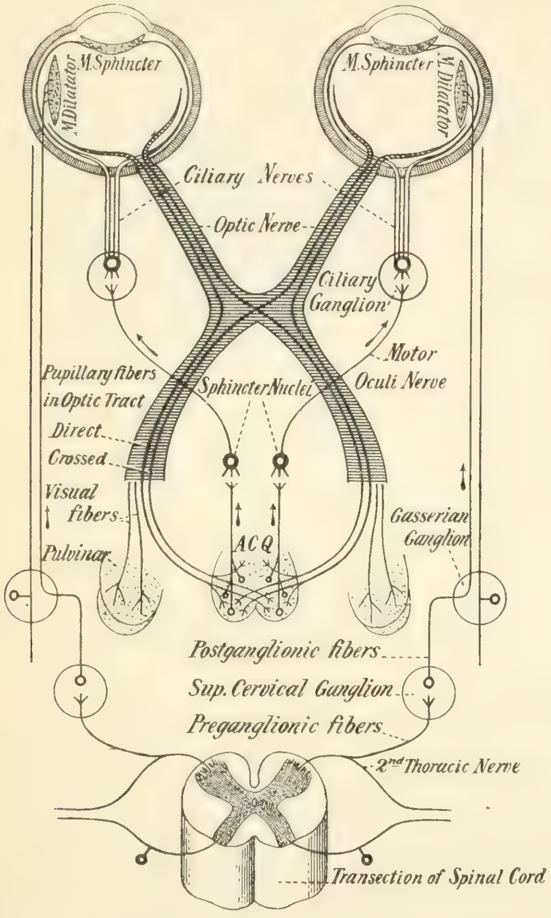
M.Dilatator
M.Sphincter
M.Sphincter
M.Dilatator
Ciliary Nerves
Optic Nerve
Ciliary Ganglion
Motor Oculi Nerve
Pupillary fibers in Optic Tract
Sphincter Nuclei
Direct
Crossed
Visual fibers
Gasserian Ganglion
Pulvinar
ACQ
Postganglionic fibers
Sup. Cervical Ganglion
Preganglionic fibers
2nd Thoracic Nerve
Transection of Spinal Cord

Fig. 268.—Diagram Designed to Show the Mechanism of the Iris Reflex. The central termination of the pupillary fibers is hypothetical.

As stated in a preceding paragraph the central termination of the afferent pupillary fibers concerned in this reflex is not positively known. No one has as yet succeeded in tracing these fibers directly to the sphincter nucleus. It has been shown, however, that as the optic tract approaches its termination the visual and the pupillary fibers separate and it has been assumed that the latter come into anatomic relation with some intercalated system which in turn is connected with the sphincter nucleus. As to the situation, origin and course of this system nothing positively is known. There is some evidence for the view that this intercalated system has its origin in the anterior corpora quadrigemina as shown in the accompanying diagram.

The contraction of the sphincter and a diminution in the size of the pupil may be direct, as when the light which enters one eye causes a reflex contraction of the sphincter of one and the same side; or it may be indirect or consensual, as when the light, which enters one eye only, causes a contraction of the sphincter not only in the eye of the same, but in the eye of the opposite side also. It is, however, highly probable that all reflex contractions of the sphincter muscles are consensual, that is, bilateral reflex actions because of the decussation of the pupillary fibers at the chiasm. Contraction of both pupils also occurs as an associated movement in the convergence of the eyes during accommodation.

The dilatation of the pupil is, however, not due exclusively to the relaxation of the sphincter pupillæ muscle, but partly to the contraction of the dilatator pupillæ muscle, which is kept normally in a state of tonic contraction by impulses emanating from a nerve-center in the medulla oblongata.

The axons which arise in this center pass down the cord, emerge through the first thoracic nerve, and then ascend to the superior cervical ganglion (see Fig. 268), in which their terminal branches arborize around its nerve-cells. From these cells new axons of the sympathetic system arise which pass successively to the ophthalmic division of the fifth nerve, the nasal nerve, the long ciliary nerve and the iris.

Experimental research renders it highly probable that the dilatator center is in a state of continuous activity and the dilatator muscle in a state of tonic contraction. Whatever the normal stimulus may be, the center is increased in activity by dyspneic blood, by severe muscle exercise, by emotional excitement, and by stimulation of various sensor nerves. That the efferent pathway just alluded to transmits the impulses to the iris is shown by the fact that division in any part of the course is followed by narrowing, stimulation, by active dilatation of the pupil.

The variations in size of the pupil, though largely a reflex act under the control of the oculo-motor nerve, are nevertheless partly due to the active coöperation of the dilatator nerves and their related muscle. The size of the pupil necessary from moment to moment for the admission of just that amount of light essential to the formation and perception of a distinct image is the result of two nicely adjusted and delicately balanced forces.

Wernicke's Hemianopic Pupillary Reaction.—It was stated on page 617 that a modification of the pupillary reaction is observed in some cases of hemianopsia, which indicates approximately the seat of the lesion. This reaction, or inaction as it is sometimes called, is present when the lesion is along the course of the optic tract between the chiasma and the anterior quadrigeminal body. In a case of left lateral hemianopsia, the lesion being in the right optic tract, the method of testing for the reaction is as follows: The eye of the left side is first carefully shielded from the light. A fine ray of light is then projected into the right eye in such a manner that it falls entirely on the non-sensitive (the temporal) side of the retina. There will be an absence of the usual pupillary response, or rather the pupil remains inactive; but if the light is gradually directed toward the sensitive (the nasal) side of the retina, there will come a moment, as the central line is crossed and the light falls on the sensitive side, when the usual pupillary response manifests itself, viz.: a contraction of the sphincter pupillæ and a diminution in the size of the pupil. The explanation of these facts will become apparent from an examination of Fig. 268 in which the course of the pupillary fibers is shown and especially if it be accepted that these fibers at their central terminations decussate or are in relation either directly or indirectly with the **sphincter centers.**

The eye of the right side is then in turn shielded from the light and the same method of examination is carried out. In this case, however, the light is projected first on the nasal, which is the non-sensitive side of the retina; there will again be no response in the pupil. But if the light is gradually directed toward the sensitive (the temporal) side, there will come a moment, as the central line is crossed and the light falls on the sensitive portion of the retina, when the usual pupillary response manifests itself. The course of the pupillary fibers in this instance will also become apparent from an examination of Fig. 268. It is evident, however, that in either case a bilateral pupillary reaction will follow stimulation of the sensitive side of either eye because of the central decussation of the pupillary fibers.

THE FOURTH NERVE. THE TROCHLEAR

The fourth cranial nerve, the trochlear, consists of peripherally coursing axons which serve to bring the cells from which they arise into relation with the superior oblique muscle.

Origin.—The axons of this nerve arise from a group of cells located beneath the aqueduct of Sylvius just posterior to the last nucleus of the third nerve. After emerging from the nucleus the nerve-fibers pass downward for a short distance, then curve dorsally around the aqueduct of Sylvius, and enter the valve of Vieussens, where they completely decussate with the nerve-fibers of the opposite side.

Cortical Connections.—The nucleus of the trochlear nerve is in histologic and physiologic connection with the motor area of the cerebral cortex. Nerve-cells in this region give off axons which enter the pyramidal tract and descend through the internal capsule and the crus cerebri, after which they cross to the opposite side. Their end-tufts arborize around the cells of the nuclei already described.

Distribution.—After its decussation the nerve-trunk emerges just below the posterior quadrigeminal body, crosses the superior cerebellar peduncle, and winds around the crus cerebri to the anterior border of the pons Varolii. It then enters the orbit cavity through the sphenoid fissure and finally terminates in the *superior oblique* muscle. In its course the nerve receives filaments from the cavernous plexus of the sympathetic and the ophthalmic division of the trigeminal.

Properties.—*Stimulation* of the nerve-trunk is followed by spasmodic contraction of the superior oblique muscle, the anterior pole of the eyeball being turned downward and outward, combined with slight torsion away from the middle line.

Division of the nerve is followed by a relaxation or paralysis of the muscle. In consequence of the now unopposed action of the inferior oblique muscle, the anterior pole of the eyeball is turned *upward* and *inward* with slight torsion toward the middle line. The diplopia consequent upon this paralysis is homonymous, the images appearing one above the other. The image of the paralyzed eye is below that of the normal eye and its upper end inclined toward that of the normal eye.

Function.—The function of the trochlear nerve is to transmit nerve impulses to the superior oblique muscle and to excite it to contraction.

THE FIFTH NERVE. THE TRIGEMINAL

The fifth cranial nerve, the trigeminal, consists of both afferent and efferent axons which for the most part are separate and distinct. The afferent axons constitute by far the major portion, the efferent fibers the minor portion, of the nerve.

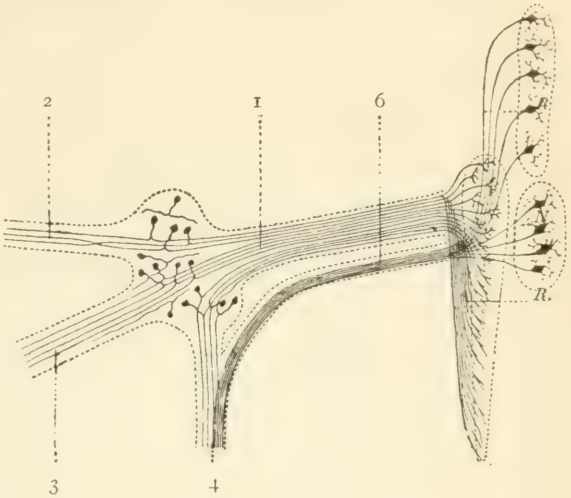

Fig. 269.—Scheme of Origin and Constitution of the Trigeminal Nerve. 1. Centrally coursing fibers. 2, 3, 4. Peripherally coursing fibers of the cells of the ganglion of Gasser. *R*, *N*. Nuclei of origin of the efferent fibers. 6. Motor root. Central terminations of the large root.

Origin of the Afferent Axons.—The afferent axons have their origin in the monaxonic cells in the ganglion of Gasser, which rests on the apex of the petrous portion of the temporal bone. The cells of this ganglion give origin to a short process which soon divides into two branches, one of which passes centrally, the other peripherally (Fig. 269). The centrally directed branches collectively form the so-called large or sensor root; the peripherally directed branches collectively constitute the three main divisions of the nerve: viz., the ophthalmic, the superior maxillary, and the inferior maxillary. Branches of the carotid plexus of the sympathetic enter the nerve in the neighborhood of the ganglion of Gasser and accompany some of its branches to their terminations.

Distribution.—1. *The Central Branches.*—The axons of the large root pass backward into the pons Varolii on its lateral aspect. After entering the pons each axon divides into two branches, one of which passes upward a short distance, the other passes downward, descending as far as the second cervical segment. Both branches give off a number of collaterals, some of which terminate in fine end-tufts around nerve-cells in the substantia gelatinosa.

2. *The Peripheral Branches.*—The peripheral axons emerge from the peripheral end of the ganglion of Gasser in three distinct and separate branches, each of which is distributed to a different region of the face and head.

1. The *ophthalmic branch* passes forward and subdivides into three large branches, the frontal, the lachrymal, and the nasal. The ultimate termination of the branches of these nerves is as follows: viz., the conjunctiva and skin of the upper eyelid, the cornea, the skin of the forehead and the nose, the lachrymal gland and caruncle, and the mucous membrane of the nose.

2. The *superior maxillary branch* passes forward through the foramen rotundum, crosses the spheno-maxillary fossa, enters the infra-orbital canal, and emerges at the infra-orbital foramen. In its course it gives off a number of branches which are distributed as follows: viz., to the integument and conjunctiva of the lower lid, the nose, cheek, and upper lip, the palate, the teeth of the upper jaw, and the alveolar processes.
3. The *inferior maxillary branch* passes through the foramen ovale, after which it subdivides into three branches—the auriculo-temporal, the lingual, and the inferior dental. The ultimate branches are distributed as follows: viz., the external auditory meatus, the side of the head, the mucous membrane of the mouth, the anterior portion of the tongue, the arches of the palate, the teeth and alveolar process of the lower jaw and the integument of the lower part of the face.

The afferent axons thus serve to bring into relation the skin, mucous membranes of the head and face, and other sentient structures, with certain sensor end-nuclei in the pons, medulla oblongata, and adjoining structures.

Cortical Connections.—The afferent portion of the trigeminal nerve is brought into physiologic relation with the sensor portion of the cerebral cortex by means of nerve-fibers which have their origin in the cells around which the terminal branches of the centrally coursing fibers arborize. The cells situated in the substantia gelatinosa give off axons, which after a short course cross the median line, enter the fillet and then ascend in the general sensor tract to the cortex where they in turn arborize around sensor nerve-cells.

Properties.—Irritative pathologic lesions, *e.g.*, pressure by tumors, aneurysms, neuritis, degenerative changes in the ganglion cells, or lesions which in any way gradually impair the physical or chemic integrity of the nerve-fibers, give rise to a variety of painful sensations referable to the seat of the lesion or to one or more regions in the peripheral distribution of the nerve. Many of the various forms of trigeminal neuralgia are caused by lesions of this character. Exposure of the dental nerves from caries of the teeth, the presence of minute foreign bodies in the conjunctiva, operative procedures in the nasal chambers, all testify to the extreme sensibility of the nerve. Division of the *large root* within the cranium is followed at once by complete abolition of all sensibility in the head and face to which its branches are distributed. The skin and mucous membranes, the eye, nose, or teeth may be experimentally injured without any evidences of pain on the part of the animal. Various reflexes, *e.g.*, those of mastication, insalivation, deglutition, the afferent paths of which are formed in part by the fifth nerve, are often seriously impaired. At the same time the lachrymal secretion diminishes and the pupil contracts. The same results are observed in human beings in whom the nerve has been divided for relief from severe neuralgia. Anesthesia or a loss of sensibility may also be caused by pathologic lesions of the nerve-trunks or of the sensor end-nuclei.

Division of the large root at or near the ganglion of Gasser has not infrequently been followed by an alteration in the nutrition of the eye and nose. In the course of twenty-four hours the eye becomes vascular and inflamed; the cornea becomes opaque; and ulceration sets in, which may lead to complete destruction of the eyeball. The mucous membrane of the nose becomes swollen, vascular, and liable to hemorrhage on the slightest irritation. The degenerative changes may lead to a complete loss of smell. These results were formerly attributed to a loss of *trophic* influence which it was believed the nerve exercised over these structures. Modern experimentation and various surgical procedures have demonstrated that the nutritive disorders are septic in origin, made possible by the anesthetic condition and by the changed vascular supply from division of the vasomotor fibers which join the nerve at or near the ganglion.

Origin of the Efferent Axons.—The efferent axons arise for the most part from nerve-cells located in the gray matter beneath the upper half of the floor of the fourth ventricle. A group of cells known as the superior or accessory nucleus, situated posterior to the corpora quadrigemina, gives origin to axons which descend and join the axons from the chief motor nucleus (Fig. 269).

Distribution.—From their origin the fibers pass forward through the pons and emerge on its lateral aspect, forming the so-called small root of the fifth nerve. This then passes forward beneath the ganglion of Gasser, leaves the cavity of the skull through the foramen ovale, and joins the inferior maxillary division already described. Its axons are ultimately distributed to the muscles of mastication: viz., the masseter, the temporal, the external and internal pterygoids, the mylohyoid, and the anterior portion of the digastric. A few axons are also distributed to the tensor tympani and tensor palati muscles. The efferent or peripherally coursing axons thus serve to bring the nerve-cells from which they arise into relation with the muscles of mastication.

Cortical Connections.—The nuclei of origin of the small root are in histologic and physiologic relation with the lower third of the motor area of the cerebral cortex. Nerve-cells in this region give off axons which enter the pyramidal tract, descend through the internal capsule and the crus cerebri, after which they cross to the opposite side. Their end-tufts arborize around the cells of nuclei in the medulla oblongata.

Properties.—*Stimulation* of the small root gives rise to convulsive movements of the muscles of mastication. *Division* of the nerve is followed by a paralysis of these muscles. Contraction or paralysis of the tensor tympani and tensor palati muscles would also be observed under the same conditions.

Functions.—The function of the afferent fibers of the fifth nerve is the transmission of nerve impulses from its peripheral distribution to (a) the medulla oblongata; (b) through its afferent cortical tracts to the cerebral cortex where they evoke sensations. The nerve therefore endows all the parts to which it is distributed with sensibility.

The function of the efferent fibers is the transmission of nerve impulses from the cells from which they take their origin, to the muscles of mastication, which are excited to activity by them. The afferent nerves are in relation centrally with the nuclei of origin of the efferent nerves, hence the latter can be excited not only voluntarily but reflexly as in the usual acts of mastication. The afferent fibers from the mouth doubtless assist in the reflex secretion of saliva.

Peripheral stimulation of different areas in the distribution of the afferent fibers, *e.g.*, conjunctiva, nasal and oral mucous membranes, teeth, etc., causes a variety of reflex activities in the muscles associated with the eyes, face, the respiratory and cardiac mechanisms, which indicate that the afferent fibers are centrally in relation with a number of motor nerve-centers.

THE SIXTH NERVE. THE ABDUCENT

The sixth cranial nerve, the abducent, consists of peripherally coursing axons which serve to bring the nerve-cells from which they arise into relation with the *external rectus* muscle.

Origin.—The axons arise from a group of cells located in the gray matter beneath the upper half of the floor of the fourth ventricle. It is quite probable that a few fibers in each nerve-trunk come from the nucleus on the opposite side of the middle line.

Distribution.—The nerve-fibers pass forward from their origin through the gray and white matter and emerge through the groove between the medulla oblongata and the pons Varolii just external to the anterior pyramid. The nerve then passes through the sphenoid fissure into the orbit cavity, where it is distributed to the *external rectus* muscle. In its course the nerve receives filaments from the carotid plexus of the sympathetic.

Cortical Connections.—The nucleus of the sixth nerve is in histologic and physiologic connection with the motor area of the cerebral cortex. From nerve-cells in this region axons are given off which enter the pyramidal tract, descend through the internal capsule and crus cerebri, after which they cross to the opposite side, where their end-tufts arborize around the cells of the nucleus already described.

Properties.—*Stimulation* of the nerve is followed by spasmodic contraction of the external rectus muscle and external deviation of the eyeball. *Division* of the nerve is followed by paralysis or relaxation of the muscle. As a result of the unopposed action of the internal rectus the anterior pole of the eyeball is turned toward the middle line (internal strabismus). In consequence of this deviation there is homonymous diplopia. The images are on the same level and parallel. The image of the paralyzed eye lies external to that of the normal eye.

Function.—The function of this nerve is to transmit nerve impulses to the external rectus muscle and excite it to contraction.

THE SEVENTH NERVE. THE FACIAL

The seventh cranial nerve, the facial, consists of peripherally coursing nerve-fibers, which serve to bring the nerve-cells from which they arise into relation with most of the superficial muscles of the head and face.

The muscles supplied by this nerve, as stated by the general anatomists, are as follows: The occipito-frontalis, corrugator supercilli, orbicularis palpebrarum, levator labii superioris alæque nasi, zygomatici, the pyramidalis nasi, compressor nasi, depressor alæ nasi, levator anguli oris, buccinator, orbicularis oris, depressor anguli oris, depressor labii inferioris, levator menti, posterior belly of the digastric, stylohyoid, and platysma myoides. These muscles by their individual and coöperative contraction express ideas and feelings and are therefore termed muscles of expression.

Origin.—The nerve-fibers or axons composing the seventh nerve arise for the most part from a nucleus of large multipolar nerve-cells situated about five millimeters beneath the upper half of the floor of the fourth ventricle toward the middle line.

From this nucleus, which is about four millimeters long, axons emerge which at first pass inward and backward as far as the ependyma of the ventricle; they then turn on themselves, forming an arch that encloses the nucleus of the sixth nerve; they then course downward and outward, emerging from the pons at its lower border between the olivary and restiform bodies. As the axons approach the floor of the ventricle collateral branches are given off which, crossing the median line, arborize around the nerve-cells of the opposite facial nucleus.

Clinic observations and histologic investigations, however, render it probable that the fibers distributed to the occipito-frontalis, the corrugator supercilii, and the upper half of the orbicularis palpebrarum, are derived from the oculo-motor nucleus, and, descending the posterior longitudinal bundle, enter the trunk of the facial as it turns to pass forward through the pons. It is also probable, for similar reasons, that the fibers distributed to the orbicularis oris are derived from the hypoglossal nucleus.

Cortical Connections.—The nucleus of the facial nerve is in histologic and physiologic connection with the facial region of the general motor area of the cerebral cortex. From the cells of this region axons descend through the pyramidal tract, the internal capsule, and the crus cerebri, beyond which they cross to the opposite side and arborize around the cells of the nucleus already described.

Distribution.—From its superficial origin the trunk of the nerve passes into the internal auditory meatus beside the auditory nerve. After passing forward and outward for a short distance through the bone above and between the cochlea and vestibule, the nerve makes a sharp bend, forming the genu facialis, turns backward and enters the aqueduct of Fallopius, the general course of which it follows as far as the stylo-mastoid foramen. After emerging from this foramen the nerve passes downward and forward as far as the parotid gland, within which it terminates by dividing into two main branches, the temporo-facial and the cervico-facial, the ultimate branches of which are distributed as previously stated to the superficial muscles of the head and face.

Properties.—*Electric stimulation* of the trunk of the nerve after its emergence from the stylo-mastoid foramen produces convulsive movements in all the muscles to which its branches are distributed. The same results follow stimulation of the intra-cranial portion of the nerve in an animal recently killed.

Irritative pathologic lesions—e.g., tumors, aneurysms, etc.—situated along the course of the nerve or at its nuclear origin, or in the cortical or sub-cortical regions, frequently give rise to spasmodic movements of the facial muscles on one side, which may be tonic or clonic in character.

Division of the facial nerve after its emergence from the stylo-mastoid foramen is followed by a complete relaxation or paralysis of the superficial facial muscles of the corresponding side. The same result follows compression of the nerve-trunk in any part of its intra-cranial course.

The phenomena presented by an individual suffering from division or compression of the facial nerve, and which collectively constitute facial *paralysis*, are as follows: A relaxed and immobile condition of the side of the face corresponding to the lesion; separation of the eyelids from paralysis of the orbicularis palpebrarum and the unopposed contraction of the levator palpebræ muscle; abolition of the ability to wink; drooping of the angle of the mouth; an escape of saliva from the mouth; contraction of the muscles and distortion of the opposite side of the face; on attempting to laugh or talk the distortion of the face is increased; during mastication the food accumulates between the teeth and cheek, from paralysis of the buccinator; articulation is impaired from paralysis of the orbicularis oris muscle, the labial sounds especially being imperfectly produced.

Functions.—The function of the facial nerve is the transmission of nerve impulses from the nerve-cells in which it arises to the superficial muscles of the face, those more especially concerned in the expression of the feelings. By reason of the association of the cortical facial area and the nucleus of origin of the facial nerve the latter becomes the medium of communication between the cortical area and the facial muscles and serves for the transmission to the muscles of those nerve impulses developed by and associated with psychic states. The muscles thus excited to action individually and collectively express in a general way the character of the psychic state. For this reason the facial nerve is termed the nerve of expression.

Branches of the Facial Nerve; Their Origin, Properties and Functions.—The branches usually described in works on anatomy as coming from the facial nerve are as a matter of fact, not branches of the facial nerve proper (with one exception, viz.: the tympanic) but are branches of autonomic nerves (vaso-motor and secretor) which after leaving the central nerve system enter the sheath of the facial. After a short distance, however, they leave it to be distributed around sympathetic ganglia. In one of these branches (the chorda tympani) afferent nerve-fibers are present which minister to the sense of taste. These fibers very naturally cannot be regarded as integral parts of the facial proper.

Between the facial and the acoustic nerve there is a small nerve known as the *pars intermedia*, the *nervus intermedius* or the *nerve of Wrisberg*. The true nature of this nerve has long been a subject of investigation. The results of histologic investigation and physiologic experimentation would indicate that it is composed of both efferent and afferent fibers. The *efferent fibers* which constitute in part the nerve of Wrisberg have their origin in a group of cells situated beneath the floor of the fourth ventricle near the median line between the nucleus of the facial and the nucleus of the motor root of the trigeminal nerve and known as the *nucleus salivatorius*. The *afferent fibers* arise from nerve-cells composing in large part the ganglionic enlargement found on the genu of the facial nerve at the point where it turns backward to enter the aqueduct of Fallopius. The cells of this geniculate ganglion, originally bipolar present single axons which soon divide into centrally and peripherally coursing branches. The centrally coursing branches constitute in part the nerve of Wrisberg, which entering and passing through the pons terminates directly or indirectly around the sensor end-nucleus of the glosso-pharyngeal nerve. The peripherally coursing branches enter the sheath of the facial nerve and accompany it as far as a point about 5 millimeters above the stylo-mastoid foramen.

From its mode of origin, the nerve of Wrisberg cannot be regarded as an integral part of the facial nerve proper, but must be considered as an independent nerve composed of both afferent and efferent fibers.

At the beginning and in the course of the aqueduct of Fallopius the facial trunk gives off the following branches: the large superficial petrosal, the small superficial petrosal, the stapedius and the chorda tympani (Fig. 270).

1. The *large superficial petrosal* nerve is given off near the geniculate ganglion. It then passes forward into the spheno-maxillary fossa and becomes associated with the spheno-palatine or Meckel's ganglion. In its course it receives a filament known as the deep petrosal, from the carotid plexus of the sympathetic. The nerve-trunk formed by the union of these two nerves is known as the Vidian nerve and terminates as stated above. The character and function of the large petrosal nerve have been a subject of much discussion. As the outcome of modern methods of investigation it may be concluded that it is composed mainly, if not entirely, of fine medullated nerve-fibers which are the continuations of corresponding fibers in the nerve of Wrisberg and that their destination is the spheno-palatine ganglion, around the nerve-cells of which their terminal branches arborize.

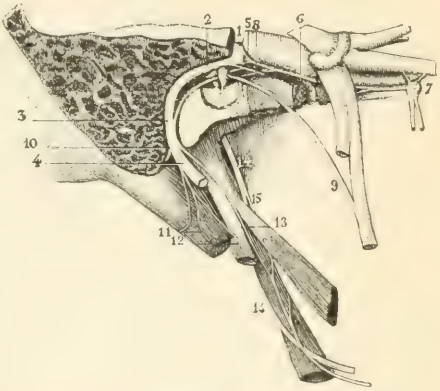

FIG. 270.—CHORDA TYMPANI NERVE. 1, 2, 3, 4. Facial nerve passing through the aqueductus Fallopii. 5. Gangliform enlargement. 6. Great petrosal nerve. 7. Spheno-palatine ganglion. 8. Small petrosal nerve. 9. Chorda tympani. 10, 11, 12, 13. Various branches of the facial. 14, 14, 15. Glosso-pharyngeal nerve.—(*Hirschfeld.*)

   Stimulation of the large petrosal, with induced electric currents, gives rise to a dilatation of the blood-vessels of, and a secretion from the mucous membrane, of the nose, soft palate, upper part of the pharynx, roof of the mouth, gums, and upper lip—the regions of distribution of the post-ganglionic fibers of cells of the spheno-palatine ganglion (see page 647). The nerve therefore contains both vaso-dilatator and secretor fibers which belong to the autonomic system of nerves. As after the administration of nicotine stimulation of this nerve is without effect, and as stimulation of the spheno-palatine ganglion gives rise to the usual vaso-dilatator and secretor effects it may be inferred that the ganglion is the way station between the pre-ganglionic fibers and the blood-vessels and glands. The deep petrosal, which joins the large petrosal is in all probability a vaso-constrictor nerve coming from the superior cervical ganglion of the sympathetic. There is no evidence that the large petrosal contains any fibers from the facial proper for the innervation of any striated muscle of the palate.

2. The *small superficial petrosal* nerve is given off from the facial at a point somewhat external to the large petrosal nerve. In its course it is joined by a small filament derived from Jacobson's branch of the glosso-pharyngeal. Together they pass into the otic ganglion, where

the fibers arborize around the nerve-cells composing it. Experiments are lacking as to the function of the small petrosal. The small size of its nerve-fibers and their termination would lead to the conjecture that they are probably vaso-dilatator and secretor. Stimulation of Jacobson's nerve gives rise to a dilatation of the blood-vessels of, and secretion from, the mucous membrane of the cheek, lips, and gums and of the parotid and orbit glands, the regions of distribution of the post-ganglionic fibers of the otic ganglion. This nerve therefore contains both vaso-dilatator and secretor fibers (see pages 155, 634).

3. The *tympanic* nerve or *stapedius* nerve is distributed directly to the stapedius muscle, and as this muscle is of the striated or skeletal variety it is innervated by the facial proper.
4. The *chorda tympani* nerve is given off from the facial at a point about 5 millimeters above the stylo-mastoid foramen. It then passes upward and forward and enters the tympanum through the iter chordæ posterius, crosses the tympanic membrane between the malleus and incus, leaves the tympanum by the iter chordæ anterius or canal of Huguier, and finally joins the lingual branch of the fifth nerve. Some of its fibers can be traced to the mucous membrane of the dorsum of the tongue, others to the submaxillary and sublingual ganglia with which they become associated.

The determination of the origin, course, and functions of the chorda tympani nerve has given rise to many investigations and discussions, and it cannot be said that the results thus far attained are as satisfactory as might be desired.

If the chorda tympani nerve is divided there follows a contraction of the blood-vessels in the neighborhood of and a diminution in the secretion from the submaxillary and sublingual glands. *Stimulation* of the peripheral end of the divided nerve gives rise to a dilatation of the blood-vessels and an increased production and discharge of saliva from these glands (see page 153). From these results it is certain that the chorda tympani contains both vaso-dilatator and secretor fibers. Nicotin applied to the submaxillary and sublingual ganglia abolishes the effects of stimulation of the chorda tympani. It does not prevent the same effects when the ganglia themselves are stimulated. It is clear, therefore, that the vaso-dilatator and secretor fibers arborize around the cells of the ganglia and are not distributed directly to the gland structures. It is highly probable that the vaso-dilatator and secretor fibers in the chorda tympani are the continuations of the efferent fibers found in the pars intermedia and that they too have their origin in the nucleus salivatorius.

If the nerve be *divided* as it crosses the tympanic cavity or before it unites with the lingual branch of the fifth nerve, there follows a loss of taste in the anterior two-thirds of the tongue on the corresponding side, though the sensibility remains unimpaired. For this and other reasons, the chorda tympani has long been regarded as the nerve of taste for this region. The nerve-fibers subserving the sense of taste are believed to be the peripherally coursing fibers which have their origin in the nerve-cells of the geniculate ganglion and which descending in the aqueduct of Fallopius are continued as the chorda tympani. The nerve impulses developed in the peripheral terminations of this nerve by the action of organic matter in solution are transmitted through the chorda tympani, along the facial nerve as far as the geniculate ganglion. The exact pathway for these *afferent* or gustatory fibers beyond the geniculate ganglion has long been a subject of much discussion. According to some observers these fibers enter the great petrosal nerve, pass forward as far as the spheno-palatine ganglion, then into the superior maxillary division of the trigeminal, and so to the brain. According to others, these fibers pass into the pars intermedia, into the pons, where they terminate around the sensor end-nucleus of the glosso-pharyngeal. The evidence for and against either of these two views is most conflicting and insufficient to justify positive statements one way or the other. To the writer the weight of evidence seems to favor the view that the gustatory fibers have their origin in the geniculate ganglion; that they pass centrally through the pars intermedia; that they are similar in function to the glosso-pharyngeal; and that they are indeed but aberrant branches of this nerve.

THE EIGHTH NERVE. THE ACOUSTIC

The eighth cranial nerve, the acoustic, consists of the centrally coursing axons of neurons which connect the essential organ of hearing with sensor end-nuclei in the pons Varolii. This nerve consists of two portions: viz., a *cochlear* or auditory and a *vestibular* or equilibratory.

Origin.—The axons comprising the cochlear portion have their origin in the bipolar nerve-cells of the spiral ganglion located in the spiral canal near the base of the osseous lamina spiralis (Fig. 271). From this origin they pass centrally into the central canal of the modiolus, at the base of which they emerge in well-defined bundles and enter the internal auditory meatus. Dendritic processes from these cells pass peripherally to terminate on the ciliated epithelial cells of the organ of Corti.

The axons comprising the vestibular portion have their origin in the bipolar nerve-cells of the ganglion of Scarpa located in the internal auditory meatus. From this origin they pass centrally in connection with the cochlear portion. Dendritic processes from these cells pass peripherally into the internal ear, where they terminate in the epithelial cells situated on the inner surface of the utricle and saccule and in the ampullæ of the semicircular canals.

The common trunk of the auditory nerve, consisting of both cochlear and vestibular divisions after emerging from the internal auditory meatus, passes backward, inward, and downward as far as the lateral aspect of the pons where the two divisions again separate.

The cochlear nerve, the external root, passes to the outer side of the restiform body and enters the ventral acoustic nucleus and the lateral acoustic nucleus, around the cells of which its end-tufts arborize. The vestibular nerve, the internal root, passes on the inner side of the restiform body to the dorsal portion of the pons, where, after bifurcating, the end-tufts of the axons arborize around the dorso-internal or chief auditory nucleus and the dorso-external or Deiters' nucleus. Some of the fibers of the vestibular branch descend through the pons and medulla as far as the cuneate nucleus.

Cortical Connections.—From the nerve-cells of the ventral and lateral acoustic nuclei axons arise, some of which cross the median plane to enter the lateral lemniscus for fillet of the opposite side, while others enter the lemniscus of the same side. The lemniscus then passes upward to the internal geniculate body around the nerve cells of which its fibers terminate. From the geniculate body the acoustic radiation arises which then passes upward and outward through the posterior limits of the internal capsule to terminate finally around the cells of the super-temporal convolution.

From the nuclei around which the vestibular branch terminates, axons arise which in all probability pursue a somewhat similar course and terminate in the temporal lobe.

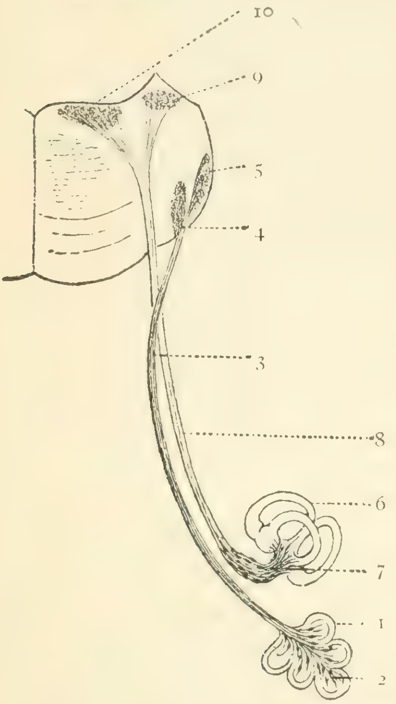

Fig. 271.—Origin and Termination of the Acoustic Nerve. 1. Cochlea. 2. Spiral ganglion (Corti). 3. Cochlear nerve. 4. Ventral acoustic nucleus. 5. Lateral acoustic nucleus. 6. Semicircular canals. 7. Ganglion of Scarpa. 8. Vestibular nerve. 9. Dorso-external nucleus (Deiters). 10. Dorso-internal nucleus.—(*After Morat and Doyon.*)

Properties.—Stimulation of the cochlear nerve is unattended by either motor or sensor phenomena. *Division* of the nerve is followed by a loss of the sense of hearing. Irritative pathologic lesions give rise to sensations of sound of varying character and intensity. Degeneration of the nerve or destruction by tumors, etc., will also be followed by a loss of the sense of hearing.

Experimental lesions of the semicircular canals involving a destruction of the physiologic relations of the *vestibular* nerve are followed by a loss of the coördinating and equilibratory power. Disordered movements, such as rotation to the right or left, somersaults backward and forward, follow destruction of these canals. Pathologic lesions in the peripheral distribution of the nerve are attended in man by disturbances of equilibrium, *e.g.*, vertigo, or a sense of swaying, pitching, and staggering.

Functions.—The function of the cochlear nerve is to convey nerve impulses from its origin to the pons, from which they are transmitted by the auditory tract to the acoustic area in the cerebral cortex where they evoke sensations of sound and its different qualities, intensity, pitch, and timbre. The specific physiologic stimulus to the development of these impulses is the impact of atmospheric undulations on the tympanic membrane, received and transmitted by the chain of bones to the structures of the internal ear—the organ of Corti—with which the peripheral terminations of the nerve are connected.

The function of the vestibular nerve is the transmission of nerve impulses to the pons, whence they are transmitted to the cortex of both the cerebrum and cerebellum and to other centers. The specific physiologic stimulus is supposed to be a variation in pressure in the ampullæ of the semicircular canals caused by inertia of the endolymph during changes in the position of the head and body. The impulses carried by the vestibular nerve give rise reflexly to certain adaptive and protective movements by which the equilibrium of the body in both dynamic and static conditions is maintained.

THE NINTH NERVE. THE GLOSSO-PHARYNGEAL

The ninth cranial nerve, the glosso-pharyngeal, consists, as shown by both histologic and experimental methods of research, of both afferent and efferent nerve-fibers, of which the former, however, are by far the more abundant. Near its exit from the cavity of the skull the nerve presents two ganglionic enlargements known as the *petrosal* and *jugular* ganglia.

Origin of the Afferent Fibers.—The afferent fibers serve to bring certain end-nuclei in the medulla oblongata into anatomic and physiologic relation with portions of the mucous membrane of the tongue, pharynx, and middle ear. The afferent fibers are axons of the monaxonic cells of the petrosal and jugular ganglia. The single axon from each of these cells soon divides into two branches, one of which passes centrally, the other peripherally. The centrally directed branches collectively form the so-called roots, four or five in number, which enter the medulla between the olivary and restiform bodies. The peripherally directed branches collectively form the two main divisions, from the distribution of which, to the tongue and pharynx, the nerve takes its name.

Distribution.—The axons of the centrally directed branches after entering the medulla pass toward its dorsal aspect, where they bifurcate, give off collateral branches, and terminate in fine end-tufts in the immediate neighborhood of two groups of nerve-cells, the *sensor end-nuclei.* The axons of the peripherally directed branches, after emerging from the base of the skull through the jugular foramen, pass forward and inward under cover of the stylo-pharyngeal muscle; winding around this muscle they divide into terminal branches which are distributed to the mucous membrane of the posterior one-third of the tongue, pharynx, soft palate, uvula, and tonsils.

Origin of the Efferent Fibers.—The efferent fibers serve to bring the nerve-cells from which they arise into connection with a portion of the musculature of the fauces and pharynx. These nerve-cells are located in the lateral portion of the *formatio reticularis* at some distance below the floor of the fourth ventricle. They constitute the upper portion of a collection of the cells known as the *nucleus ambiguus.*

Distribution.—From this origin the efferent fibers pass dorsally to near sensor end-nuclei, then turn outward and forward and finally emerge from the medulla in intimate association with the afferent fibers. They are ultimately distributed to the stylo-pharyngeus, and to the middle constrictor muscle of the pharynx. In addition to the foregoing efferent fibers the glossopharyngeal nerve contains at its emergence from the medulla both vaso-motor and secretor fibers.

Jacobson's Nerve.—This is a small branch which leaves the glosso-pharyngeal at the petrous ganglion. After passing through a small canal in the base of the skull it enters the tympanic cavity, within which it gives off branches to the great and lesser petrosal nerves, to the mucous membrane of the foramen ovale, the foramen rotundum, and to the Eustachian tube.

Cortical Connections.—The *motor* nucleus is doubtless connected with the general motor area of the cortex through fibers descending in the pyramidal tract. The exact location of the cortical area for the pharynx is not well determined, but is most likely to be found in the lower part of the general motor area near the termination of the Rolandic fissure. The exact cortical connections of the afferent tract are unknown, but are most likely to be found in the general sensor area.

Properties.—Stimulation of the glosso-pharyngeal trunk with induced electric currents calls forth evidence of pain and contraction of the stylo-pharyngeus and middle constrictor muscles. Peripheral stimulation of the terminals of the nerve-fibers in the mucous membrane of the posterior third of the tongue with different kinds of organic matter in solution, develops nerve impulses which transmitted to the cortex evoke sensations of taste. Division of the nerve abolishes sensibility in the mucous membrane to which it is distributed, impairs the sense of taste in the posterior third of the tongue, and gives rise to paralysis of the above-mentioned muscles.

Stimulation of Jacobson's nerve is followed by dilatation of the blood-vessels of, and secretion from, the mucous membrane of the lower lip, cheek, and gums, and from the parotid gland. Division of the nerve is followed by the opposite results. The course of the fibers which give rise to these results is by way of the lesser petrosal to the otic ganglion, around the cells of which the fibers arborize. From the cells of this ganglion non-medullated fibers pass to the blood-vessels and gland cells. These nerve-fibers are thus members of the autonomic system of nerves.

Functions.—The afferent fibers of the glosso-pharyngeal transmit nerve impulses from the parts to which they are distributed to the cerebral cortex. where they evoke sensations of pain and sensations of taste; they also assist in all probability in the performance of certain reflexes connected with deglutition. The afferent fibers are therefore divisable into nerves of general sensibility and nerves of special sense. The efferent fibers transmit impulses to muscles, exciting them to activity, and to the otic ganglion, which in turn dilates blood-vessels and excites secretion. The fibers exciting secretion have their origin in the *nucleus salivatorius*, from which the efferent autonomic fibers in the chorda tympani nerve arise.

THE TENTH NERVE. THE PNEUMOGASTRIC OR VAGUS

The tenth cranial nerve, the pneumogastric or vagus, consists, as shown by histologic methods of research, of both afferent and efferent fibers, independent of those derived in its course from adjoining motor or efferent nerves. Near the exit of the nerve from the cavity of the cranium it presents two ganglionic enlargements known respectively as the ganglion of the root (the jugular) and the ganglion of the trunk (the plexiform).

Origin of the Afferent Fibers.—The afferent fibers take their origin in the monaxonic cells of the ganglia on the root and trunk. The single axon from each of these cells soon divides into two branches, one of which passes centrally, the other peripherally. The centrally directed branches collectively form the so-called roots, ten to fifteen in number, which enter the medulla between the restiform body and the lateral column. The peripherally directed branches collectively form a portion of the common trunk of the nerve.

Distribution.—The axon of the centrally directed branches after entering the medulla pass toward its dorsal aspect, where they bifurcate, give collaterals, and terminate in fine end-tufts in the immediate neighborhood of two groups of nerve-cells, the *vagal sensor end-nuclei.*

The axons of the peripherally directed branches unite to form a portion of the common trunk, which, as it descends the neck and enters the thorax and abdomen, gives off a number of branches which are ultimately distributed to the mucous membrane of the esophagus, larynx, lungs, stomach, and intestine, and also to the heart. The afferent fibers thus serve to bring into anatomic and physiologic relation the mucous membrane of these organs and certain sensor end-nuclei in the medulla oblongata.

Origin of the Efferent Fibers.—The efferent fibers take their origin from nerve-cells located in the lateral portion of the *formatio reticularis* at some distance below the floor of the fourth ventricle. These cells constitute the lower portion of the *nucleus ambiguus.*

Distribution.—From their origin the efferent axons pass dorsally to near the sensor end-nuclei, then turn outward and forward, and finally emerge from the medulla in close association with the afferent branches. They are ultimately distributed to the muscles of the lower two-thirds of the esophagus; to the muscle-fibers of the stomach and perhaps the intestines; to the walls of the gall-bladder and to the sphincter of the common bile-duct; and to the non-striated muscle-fibers of the bronchial tubes, and to the heart. Among the efferent fibers are some which are distributed to the gastric glands and to the pancreas. From this distribution it is apparent that the efferent fibers in the vagus are largely if not entirely members of the autonomic system of nerves.

The efferent fibers serve to bring the nerve-cells from which they arise into anatomic and physiologic connection with a portion of the musculature of the alimentary canal and its diverticulum, the lung as well as the heart and gastric glands.

Communicating Branches.—At or near the ganglia the vagus receives communicating branches from the eleventh nerve, the spinal accessory, the facial, the hypoglossal, and the anterior branches of the two upper cervical nerves. Owing to this manifold origin of the efferent fibers in the trunk and peripheral branches of the vagus, it is, in some instances, difficult, if not impossible, to determine to which of these nerves a given muscle contraction is to be referred

Vagal Branches.—As the vagus passes down the neck it gives off the following main branches:

1. The *pharyngeal nerves*, which, after entering into the formation of the pharyngeal plexus, are distributed to the mucous membrane and to the muscles of the pharynx; *e.g.*, superior and inferior constrictors, the levator palati, and the azygos uvulæ; according to Beevor and Horsley the nerves for these muscles are branches of the spinal accessory.
2. The *esophageal nerves*, which after entering into the formation of the esophageal plexus, are distributed to the mucous membrane, and to the muscles of the lower two-thirds of the esophagus.
3. The *superior laryngeal nerve* which, entering the larynx through the thyro-hyoid membrane, is distributed to the mucous membrane lining the interior of the larynx and to the crico-thyroid muscle. From the superior laryngeal and the main trunk small branches are given off which in the rabbit unite to form a single nerve, the so-called *depressor*

nerve. (See page 325.) It is distributed to the surface of the ventricle and perhaps to structures at the root of the aorta. Though this anatomic arrangement is not found in man, there are many reasons for believing that analogous fibers are present in the vagus trunk of man and other animals.

4. The *inferior laryngeal nerve* which is distributed ultimately to all the muscles of the larynx (except the crico-thyroid) and to the inferior constrictor of the pharynx. These motor fibers are derived from the spinal accessory.
5. The *cardiac nerves* which, after entering into the formation of the cardiac plexus, are distributed to the heart.
6. The *pulmonic nerves* distributed to the mucous membrane of the bronchial tubes and their ultimate terminations, the lobules and air-cells, as well as to their non-striated muscle-fibers.
7. The *gastric and intestinal nerves*, distributed to the mucous membrane and muscle walls of the stomach, intestines, and gall-bladder. Other fibers in all probability pass to the liver, spleen, kidney, and suprarenal bodies.

Properties of the Pneumogastric or Vagus Nerve and its Various Branches.—*Faradization* of the vagus nerve close to the medulla oblongata gives rise to sensations of pain and to contraction of the musculature of a portion of the alimentary tract, viz.: the esophagus, stomach, and possibly of the intestine and of the pulmonary apparatus, and at the same time causes an inhibition of the heart. *Division* of the nerve is followed by a loss of sensibility in the mucous membrane of the alimentary tract and of the pulmonary apparatus, together with a loss of motility of the structures above mentioned, and a loss of the inhibition of the heart.

Stimulation of the trunk of the nerve in different parts of its course produces a variety of results dependent to some extent on the presence of anastomosing branches from adjoining nerves.

The Pharyngeal Nerves.—Faradization of the pharyngeal nerves consisting of both afferent and efferent fibers, gives rise to sensations of pain, contraction of the pharyngeal muscles, and perhaps to vomiting. Division of these nerves is followed by a loss of sensibility in the parts to which they are distributed and by paralysis of the muscles with a consequent impairment of deglutition.

The Esophageal Nerves.—Faradization of the esophageal nerves, gives rise to sensations of pain and to contractions of the muscle coat of the esophagus. Division of these nerves is followed by a loss of sensibility in the parts to which they are distributed, a partial paralysis of the muscle coat and an impairment of deglutition.

The Superior Laryngeal Nerve.—Faradization of the superior laryngeal nerve gives rise to sensations of pain, and to contraction of the crico-thyroid muscle. Through reflected impulses it causes contraction of the muscles of deglutition, and of the muscles concerned in the act of coughing; inhibition of the inspiratory movement and arrest of respiration in the condition of expiratory standstill, with perhaps a tetanic contraction of the expiratory muscles, and contraction of the laryngeal muscles with closure of the glottis.

Peripheral stimulation of this nerve—*e.g.*, the contact of foreign particles—gives rise to a similar series of phenomena. Division of these nerves is followed by a loss of sensibility in the laryngeal mucous membrane, paralysis of the crico-thyroid muscle with a consequent lowering of the pitch, and a diminution in the clearness of the voice. In consequence of the loss of the sensibility there is an inability to perceive the entrance of foreign bodies into the larynx.

The Depressor Nerve.—Stimulation of the peripheral end of the depressor nerve is without effect; stimulation of the central end retards and even arrests the heart's pulsations and lowers the general blood-pressure. These two effects, though associated, are nevertheless independent of each other. If the vagus nerves be divided on both sides between the origin of the depressor and the origin of the cardiac nerves, and the former stimulated, there will be a fall of pressure without retardation of the heart. The effect on the heart is attributed to a stimulation of the cardio-inhibitor mechanism in the medulla oblongata.

The fall of general blood-pressure was formerly attributed to a sudden dilatation of the splanchnic blood-vessels alone, in consequence of a depression of that portion of the general vaso-motor center which maintains through the splanchnic nerves a tonic contraction of their walls. It has been satisfactorily demonstrated that this is not the sole cause; for after division of the splanchnic nerves, stimulation of the depressor causes a still further fall of from 30 to 40 per cent. in the general pressure (Porter and Beyer). Evidently, not any one, but all portions of the vaso-motor center are subject to the effects of depressor stimulation.

The Inferior Laryngeal Nerves.—Faradization of the inferior laryngeal nerves produces effects which vary in accordance with the strength of the stimulus, with different animals, and with the same animal at different periods of life. In the adult dog and in man, the glottis is kept widely open for respiratory purposes by the tonic contraction of the abductor muscles (the posterior crico-arytenoids); for phonatory purposes the glottis is closed and the vocal membranes approximated by the contraction of the adductor muscles. It has been shown that these opposed groups of muscles have independent nerve-supplies; that two sets of fibers in the common trunk can be separated and stimulated independently of each other. *Feeble* stimulation of the common trunk produces a still further abduction of the vocal cords. With an increase in the strength of the stimulus, however, the reverse obtains: namely, adduction which increases until the glottis is completely closed. Division of the nerves is followed by paralysis of both the phonatory and respiratory muscles, the abductors and adductors, with the result of seriously impairing both phonation and respiration and not infrequently causing death. The fibers of the inferior laryngeal nerve are derived from the eleventh nerve, the spinal accessory.

The Cardiac Nerves.—Faradization of the trunk of the vagus or of the peripheral end of the divided nerve gives rise to a diminution in the frequency and force of the heart's contractions; and if the stimulation be sufficiently powerful, completely arrests it in the phase of diastole. To these results the term inhibition is applied. Division of the vagi or of the cardiac branches is followed by an increase in the number of contractions from loss of inhibitor influences. The inhibitor fibers of the vagus are generally believed to be derived from the spinal accessory, though this has been questioned. According to the recent investigations of Schaternikoff and Friedenthal, they come direct in the vagus, from a nucleus near the vagal motor nucleus in the medulla, the spinal accessory sending no branches to the heart. In the frog and other batrachia the vagus contains also accelerator or augmentor fibers derived from the sympathetic; hence stimulation, especially if feeble, may increase the heart's action.

The Pulmonic Nerves.—The pulmonic nerves, given off from the trunk after its entrance into the thorax, do not lend themselves readily to experimentation. Division of both vagi in the neck above the point of exit of the pulmonic branches is followed by a decrease in the frequency of the respiratory acts, with an increase in their depth. At the same time there is a loss of sensibility of the mucous membrane of the trachea and lungs and a paralysis of non-striated muscle-fibers.

Stimulation of the central end of the divided vagus with weak induced electric currents increases the frequency, but decreases the amplitude, of the respiratory movements. This would indicate that in the physiologic state these nerve-fibers conduct afferent nerve impulses that inhibit the inspiratory discharge and lead to an expiratory movement sooner than would otherwise be the case. If the stimulation be increased in intensity the inspiratory movement gradually so exceeds the expiratory that the inspiratory muscles pass into the condition of tetanus and the chest walls come to rest in the condition of forced inspiration.

Stimulation of the vagus with strong induced electric currents not infrequently inhibits the inspiratory movement and increases the expiratory until there is a complete cessation of movement in the condition of expiratory standstill. The effect thus produced is similar to, if not identical with, that produced by stimulation of the superior laryngeal nerve.

Faradization of the trunks of the pulmonic branches or stimulation of their peripheral terminations in the mucous membrane of the bronchial tubes or alveoli by the inhalation of chemic vapors causes arrest of respiratory movements, a fall of blood-pressure, and a reflex inhibition of the heart (Brodie).

The Gastric Nerves.—Stimulation of the peripheral end of a divided vagus nerve causes a distinct contraction of the right half of the stomach and secretion from the gastric glands. Division of the nerve abolishes the sensibility of the mucous membrane of the stomach, impairs motility, and interferes with the secretion of the gastric juice.

Similar experimentation on the trunk of the vagus has shown that the nerve excites contraction of the upper part of the small intestine and of the gall-bladder, the secretion of the pancreas, the renal circulation, the secretion of urine, etc.

Functions.—The afferent fibers transmit nerve impulses from the area of their distribution to the medulla and thence through cortical connections to the sensor cerebral areas, where they evoke sensations. They therefore endow all parts to which they are distributed with sensibility.

The efferent fibers transmit impulses outward which excite contraction of the muscle of the lower two-thirds of the esophagus, the stomach, the small intestine, and the gall-bladder, and the muscles of the bronchial tubes; excite secretion from the glands of the stomach, pancreas, and kidney, and exert an inhibitor influence on the activity of the heart. The efferent fibers belong to the autonomic system of nerves and are not connected with the ganglia of the vagus, but with local peripheral ganglia.

The afferent fibers also assist in the maintenance of certain organic reflex actions which are highly essential to the life of the individual, *e.g.*, respiration, the heart-beat, blood-pressure, etc., all of which have been considered in foregoing pages.

THE ELEVENTH NERVE. THE SPINAL ACCESSORY

The eleventh cranial nerve, the spinal accessory, consists of peripherally coursing fibers which bring the nerve-cells from which they arise into relation with separate but functionally related muscles, such as those entering into the formation of the larynx. It consists of two portions, the medullary or bulbar and the spinal.

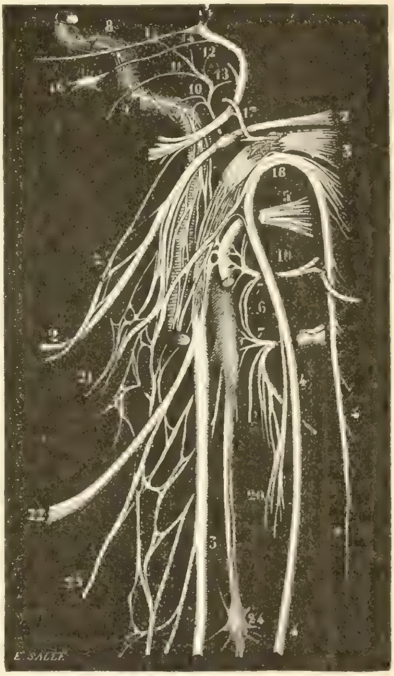

FIG. 272.—SPINAL ACCESSORY NERVE. 1. Trunk of the facial nerve. 2, 2. Glosso-pharyngeal nerve. 3, 3. Pneumogastric. 4, 4, 4. Trunk of the spinal accessory. 5. Sublingual nerve. 6. Superior cervical ganglion. 7, 7. Anastomosis of the first two cervical nerves. 8. Carotid branch of the sympathetic. 9, 10, 11, 12, 13. Branches of the glosso-pharyngeal. 14, 15. Branches of the facial. 16. Otic ganglion. 17. Auricular branch of the pneumogastric. 18. Anastomosing branch from the spinal accessory to the pneumogastric. 19. Anastomosis of the first pair of cervical nerves with the sublingual. 20. Anastomosis of the spinal accessory with the second pair of cervical nerves. 21. Pharyngeal plexus. 22. Superior laryngeal nerve. 23. External laryngeal nerve. 24. Middle cervical ganglion.—(*Hirschfeld.*)

Origin.—The axons comprising the *medullary* portion arise from a group of nerve-cells in the extreme lower part of the *nucleus ambiguus*, known as the nidus laryngei. From this origin the axons pass forward and outward to emerge from the medulla just below and in series with the roots of the vagus nerve.

The axons comprising the spinal portion have their origin in nerve-cells in the lateral margin of the anterior horn of the gray matter in the cervical portion of the cord as far down as the fifth cervical vertebra. From this origin the fibers pass to the surface of the cord to emerge between the ventral and dorsal roots in from six to eight filaments, after which they unite from below upward to form a distinct nerve. This enters the cranial cavity through the foramen magnum, where it joins with the medullary portion to form the common trunk, which then passes forward to emerge from the cranium through the jugular foramen. (Fig. 272.)

Distribution.—After emerging from the cranial cavity the nerve soon separates into two branches:

1. An *internal* or *anastomotic* branch, consisting chiefly of filaments coming from the medulla oblongata. It soons enters the trunk of the vagus, from which fibers pass through the pharyngeal plexus to the superior and inferior constrictor muscles of the pharynx, to the palato-pharyngeus, to the levator palati and azygos uvulæ muscles (Beevor and Horsley); to

the muscles of the larynx through the inferior laryngeal nerve, and to the heart according to some authorities.

2. An *external* branch, consisting chiefly of the accessory fibers from the spinal cord.

It is distributed to the sterno-cleido-mastoid and trapezius muscles.

Cortical Connections.—The nucleus of origin of the medullary branch at least, is in relation with nerve-cells in the lower third of the general cerebral motor area, the axons of which descend in the pyramidal tract.

Properties.—Faradization of the medullary portion of the nerve near its origin gives rise to contraction of the muscles to which it is distributed. Destruction of the medullary root is followed by impairment of deglutition from a paralysis of the muscles of the pharynx and palate and a loss of the power of producing vocal sounds on account of paralysis of the constrictor muscles of the larynx. According to some authorities, there is also an acceleration of the heart's action from a loss of inhibitor influences.

Stimulation of the external branch gives rise to contraction of the sterno-cleido-mastoid and trapezius muscles, though division of the branch does not give rise to complete paralysis, as they are supplied with motor fibers also from the cervical nerves. In consequence of division of the external branch animals experience extreme shortness of breath during exercise, from a want of coördination of the muscles of the fore limbs and the muscles of respiration.

Functions.—The function of the fibers of the spinal accessory nerve is the transmission of nerve impulses from the cells from which they take their origin to the muscles to which they are distributed. They therefore excite to action some of the muscles of deglutition; the muscles which regulate the tension of the vocal bands during phonation and the muscles which control the respiratory movements associated with sustained or prolonged muscle efforts. The fibers may also convey nerve impulses which exert an inhibitor influence on the heart.

THE TWELFTH NERVE. THE HYPOGLOSSAL

The twelfth cranial nerve, the hypoglossal, consists of peripherally coursing nerve-fibers which serve to connect the nerve-cells from which they arise with the musculature of the tongue.

Origin.—The axons composing the hypoglossal nerve arise from a collection of nerve-cells situated beneath the floor of the fourth ventricle. This nucleus is elongated and extends from the medullary striæ downward as far as the lower border of the olivary body. It is located ventro-laterally to the spinal canal. After leaving the cells of the nucleus the axons pass forward and outward toward the surface of the medulla, from which they emerge in ten or twelve small bundles or filaments in the groove between the olivary body and the anterior pyramid. Beyond this point they unite to form a common trunk.

Distribution.—The common trunk thus formed passes out of the cranial cavity through the anterior condyloid foramen. In its course it receives filaments from the first and second cervical nerves, the sympathetic and vagus. It is finally distributed to the intrinsic muscles of the tongue and to the genio-hyo-glossus, hyo-glossus, and stylo-hyoid muscles. Branches derived from the cervical plexus pass to muscles which elevate and depress the hyoid bone.

Cortical Connections.—The hypoglossal nerve nuclei are connected with nerve-cells in the lower third of the general motor area around the inferior termination of the fissure of Rolando by axons which descend in the pyramidal tract.

Properties.—Faradization of the nerve gives rise to convulsive movements of the muscles to which it is distributed. Division of the nerve is followed by a loss of motion and an interference with deglutition, mastication, and articulation, especially in the pronunciation of the consonantal sounds. In hemiplegia, complicated with paralysis of the tongue from injury to the hypoglossal tract, the opposite side of the tongue is involved in the paralysis. On protrusion of the tongue the tip is deviated to the paralyzed side, due to the unopposed action of the muscle of the opposite side.

Function.—The hypoglossal nerve transmits nerve impulses from its origin to the intrinsic and extrinsic muscles of the tongue, exciting them to activity. The coördinate activity of these muscles favorably assists mastication, articulation, and deglutition.

CHAPTER XXVI

THE AUTONOMIC NERVE SYSTEM

Introductory Statements.—The motor tissues of the body may be divided into two groups, the one, comprising the *striated skeletal* muscles, the other, comprising the *striated cardiac*, and the *non-striated vascular* and *visceral* muscles, and the *epithelium* of glands. The movements to which they give rise are, in the first instance, those exhibited mainly by the head, upper and lower extremities; and in the second instance, those exhibited by the heart and blood-vessels; by the walls of the viscera, *e.g.*, stomach, intestines, bile and urinary bladders, etc., and those exhibited by glands (the secretion and discharge of fluids), *e.g.*, salivary, gastric, perspiratory, mammary, etc., as well as the specific agents, *e.g.*, adrenalin, pituitrin, etc., discharged into the blood. The activities which these two groups of motor tissues exhibit are excited mainly by two ultimate and separate factors.

The Skeletal Muscles.—The skeletal muscles in the different regions of the body are excited to action by nerve impulses, which come to them directly from special groups of emissive or motor cells situated in the gray matter beneath the aqueduct of Sylvius, beneath the floor of the fourth ventricle, and in the ventral cornua of the gray matter of the spinal cord. The nerve impulses, discharged by these cells, are transmitted *directly* through but *one* axon to the muscle. The nerve-cells in these different regions, though irritable, do not possess spontaneity of action, but require for the manifestation of their activity the arrival and the stimulating influence of nerve impulses. These may come (1) from peripheral regions of the body through afferent spinal nerves in consequence of the action of external agents, in which case the resulting movement is termed a reflex movement; or (2) from the cerebrum through descending nerve-fibers in consequence of an act of volition, in which case the resulting movement is termed a volitional or voluntary movement. In the performance of daily work the skeletal muscle activities, though frequently caused by reflected nerve impulses are, in the vast majority of instances, caused by nerve impulses of cerebral (volitional) origin. From moment to moment these muscles are excited to action, guided and controlled for the most part by this dominating and in some respect arbitrary factor. By the constant exercise of the will, these muscles are compelled to act constantly, and for this reason it is said that they do not possess independent activity, except in a minor degree.

The Striated Cardiac, the Non-striated Vascular and Visceral Muscles and the Epithelium of Glands.—The striated cardiac, the vascular and visceral muscles, and the epithelium of glands in all regions of the body, if not primarily excited to action, are at least controlled and regulated in their activities, by nerve impulses that come to them indirectly from special groups of emissive or motor nerve-cells situated in (1) a small region at the extreme upper part of the gray matter beneath the aqueduct of Sylvius; (2) in special regions in the gray matter beneath the floor of the fourth ventricle;

(3) in the ventral horns of the gray matter of the spinal cord between and including the levels of origin of the second thoracic to the second or third lumbar nerves; and (4) in the gray matter of the lower portion of the cord between and including the levels of origin of the second to the fourth sacral nerves. The nerve impulses discharged by these cells are transmitted *indirectly*, not through one, but through *two* successively arranged neurons. The first, a fine white medullated fiber, emerges from the medulla or spinal cord in association with the large motor root fibers passing to the skeletal muscles, and after a variable distance leaves these fibers to arborize around and to become physiologically related to a sympathetic ganglion; the second, a fine, dark non-medullated fiber, emerges from one of the cells of the ganglion, which, after pursuing a longer or shorter course, branches and becomes histologically and physiologically related to non-striated muscle-fibers and epithelium. The first neuron is termed *pre-ganglionic*, the second *post-ganglionic*, or in accordance with long-established usage, sympathetic.

The nerve-cells in the regions which give origin to the pre-ganglionic neurons, though irritable, do not possess spontaneity of action, but require for the manifestation of their activities, the arrival and stimulating influence of nerve impulses. These may likewise come (1) from peripheral regions of the body through afferent nerves in consequence of the action of external agents—in which case the resulting movement is termed a reflex movement; or (2) from the cerebrum through descending nerve-fibers in consequence of *affective* or *emotional* psychic states, in which case the resulting movement or modification of movement, is termed an affective or an emotional movement. In the performance of the functions of vascular and visceral organs and glands, the non-striated muscles and epithelium are in the vast majority of instances caused by reflected nerve impulses, though frequently modified by nerve impulses of cerebral (affective or emotional) origin.[1]

From the fact that the nerve-centers of the pre-ganglionic nerve-fibers in the cranio-bulbar and spinal-cord regions are removed from and not subject to volitional control; and from the further fact that they are in the vast majority of instances stimulated to activity by nerve impulses transmitted from peripheral regions (though modified from time to time by the ever varying phases of affective or emotional psychic activity) this system of nerves is regarded as in a sense independent, *i.e.*, of volitional control, self-regulative or autonomous in its activity, and, therefore, has been designated the *autonomic nerve system* (Langley). The tissues to which it is distributed have also been designated the autonomic tissues.

In a consideration of this subject it must be borne in mind that there are not two nerve systems, but only one, which, however, may be subdivided into two portions, one of which in its peripheral distribution is associated directly with skeletal muscles only; the other of which is associated indirectly, through the intervention of a ganglion, with non-striated muscle and gland epithelium. The central origin of these two portions is essentially the same, and the central cells are influenced in the same way, though in different degrees, by peripheral and cerebral activities.

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[1] It is only necessary to recall the well-known effects of psychic states on the heart, on the blood-vessels and sweat-glands of the neck and face; the observations of Pavlov on the effects of agreeable psychic states on the flow of saliva and gastric juice; the observations of Cannon of the effects of psychic states of an opposite character of fear, anger, etc., on the gastric and intestinal movements and the secretion of the adrenal glands.

THE PHYSIOLOGIC ANATOMY OF THE AUTONOMIC NERVE SYSTEM

In a consideration of the essential facts of the physiologic anatomy of this system, it will be found convenient to consider first the sympathetic ganglia, and the distribution of their post-ganglionic fibers.

The Sympathetic Ganglia.—The sympathetic ganglia may for convenience of description be divided into three groups: viz., the vertebral or lateral, the pre-vertebral or collateral, and the peripheral or terminal.

The *vertebral* ganglia are arranged in the form of chains, one on each side of the vertebral column. The number of ganglia in the chain varies in animals of different and in animals of the same species. In man the number varies from 20 to 22. Each chain may be divided into a cervical, a thoracic a lumbar, a sacral, and a coccygeal portion. The cervical portion is usually described as consisting of three ganglia—a superior, a middle and an inferior. This statement is open to question, however, as the middle one is frequently absent and the inferior is regarded by some anatomists as belonging to the pre-vertebral series. The thoracic portion consists of ten or twelve ganglia, the lumbar and sacral portions of four each and the coccygeal portion of one, the so-called ganglion impar.

The *pre-vertebral* ganglia are also united in the form of a chain situated in the abdominal cavity. The ganglia constituting this chain are known as the semilunar, the renal, the superior and inferior mesenteric, and hypogastric, or pelvic.

The *peripheral* ganglia are in more or less close relation with tissues and organs in different regions of the body. Among the members of this group may be mentioned the ciliary or ophthalmic, the spheno-palatine, the otic and the submaxillary ganglia; the ganglia in the walls of the heart, in the walls of the respiratory organs, in the walls of the stomach, intestines and at the base of the bladder (the pelvic ganglia).

Structure of the Ganglia.—Each ganglion consists of a capsule or stroma of connective tissue in which are contained large numbers of nerve-cells, nerve-fibers, medullated and non-medullated, and blood-vessels. The nerve-cells give origin to two or more dendrites, which, perforating a nucleated capsule by which each cell is surrounded, branch and re-branch and interlace to form a pericapsular plexus. Each cell gives origin to an axon, which as it leaves the cell becomes invested with a sheath continuous with the capsule surrounding the cell-body. It is, however, wanting in a medullary sheath, and hence the nerve presents a gray color. Such a structure, in its entirety, is known as a sympathetic neuron. The axonic processes as they emerge from the cells become united and in many instances form distinct nerve strands, but subsequently as they approach their distribution divide and subdivide, forming smaller and even smaller bundles, which pass in different directions to regions varying in position according to the situation of the ganglion from which they come. These post-ganglionic fibers are for descriptive purposes divided into two groups, viz.: (1) the *gray rami communicantes*, and (2) the *rami viscerales*.

THE ANATOMIC RELATIONS OF THE SYMPATHETIC GANGLIA TO PERIPHERAL STRUCTURES

The Vertebral Ganglia.—1. The *grey rami communicantes.* The fibers composing these branches, as the name implies, communicate with the trunks of the spinal nerves. Each ganglion of the vertebral chain gives origin to one or more of these post-ganglionic branches which pass backward and outward and enter the sheath of the corresponding spinal nerve. In the cervical region, however, where the ganglia do not correspond in number with the cervical spinal nerves, the ganglia give off two or more gray rami. Thus in man the superior cervical ganglion sends branches to the first four cervical nerves. The middle and inferior ganglia send a branch to the fifth and sixth and the seventh and eighth cervical nerves respectively. The first thoracic ganglion sends several branches into the trunks of the nerves that enter into the formation of the brachial plexus. The ganglia in the thoracic, lumbar and sacral regions, send at least one gray ramus, in some instances two, into the sheath of the corresponding thoracic, lumbar and sacral nerves.

The gray rami which thus enter the sheath of the spinal nerve trunks, pass in company with their efferent motor fibers, to the periphery, to be finally distributed to structures in the skin, viz.: non-striated muscles of blood-vessels, non-striated muscles of hair follicles, and epithelium of sweat-glands. The blood-vessels and sweat-glands of the skin of the neck receive their ganglionic nerve-supply from the superior and middle cervical ganglia; those of the skin of the arm, from the inferior cervical and first thoracic ganglia; those for the skin of the trunk, from the thoracic ganglia; those for the skin of the hip and leg, from the lumbar and upper sacral ganglia; those for the skin of the external genital organs, from the lower sacral ganglia.

2. *The rami viscerales.*—The fibers composing these branches were supposed, as the name implies, to pass directly to viscera, though it is apparent from the course they pursue that they communicate, if not with spinal, at least with cranial nerves.

The *superior cervical* ganglion gives off from its cephalic extremity two visceral branches, which subsequently divide and subdivide forming the carotid and cavernous plexuses; from these plexuses slender branches follow the course of the more superficial arteries at least, to their terminations, while others pass into the trunks of the trigeminal, abducent, and the superior and deep petrosal branches of the facial nerve, to be distributed to blood-vessels and glands of special regions of the head and face. Still other branches pass down the neck and in their course become associated with corresponding branches from the middle and inferior cervical ganglia. Interlacing in an intricate manner they assist in forming the cardiac plexuses.

The *middle cervical* ganglion gives off visceral branches, which in association with branches from the inferior cervical ganglion, pass to the thyroid gland to be distributed to the walls of the blood-vessels and to the gland cells as well. Stöhr, Berkley and others have shown that fine non-medullated nerve filaments terminate on and between the epithelial cells lining the follicles, though the supply is not very abundant.

The *inferior cervical* ganglion gives off visceral branches which pass downward and forward and are ultimately distributed to the heart-muscle. With these fibers there are usually associated, according to the animal considered, visceral fibers which come from the first thoracic or stellate ganglion. These fibers are known as the *sympathetic cardiac* fibers and have for the physiologist and clinician great interest as they are associated with the activities of the heart. (See pages 311 and 319.)

The *thoracic, lumbar* and *sacral* ganglia also give off visceral branches which pass for the most part to neighboring structures, though from the lower lumbar and sacral ganglia branches pass to viscera in the lower abdominal and pelvic regions.

In accordance with the law of distribution and relations of the fibers of the sympathetic ganglia to peripheral organs, it can be assumed that to whatever organ the visceral branches are distributed they too ultimately terminate in the non-striated muscle-cells of the walls of the blood-vessels and the walls of hollow viscera, and in some situations in the epithelium of glands as well.

The Pre-vertebral Ganglia.—The pre-vertebral ganglia are located in the abdominal cavity.

The *semilunar*, the *renal*, and the *superior mesenteric* are situated in the neighborhood of the celiac axis and on a level with the adrenal bodies. These ganglia give off an enormous number of *visceral* branches which interlace in a very intricate manner forming what is known as the solar plexus. Subdivisions of this plexus, taking their names from the regions to which they are distributed, are known as the gastric, renal, adrenal, splenic, hepatic and superior mesenteric. The terminals of the fibers composing these plexuses are distributed to the non-striated muscle-fibers of blood-vessels of the stomach, kidney, adrenal body, liver, and small intestine; to the muscle-walls of the stomach, the small intestine, the walls of the gall-bladder, as well as the sphincter muscles surrounding the pyloric and the ileo-colic orifices.

The *inferior mesenteric* ganglion situated close to the origin of the inferior mesenteric artery gives off *visceral* fibers, which also interlace with other fibers to form the hypogastric plexus, from which fibers pass to the muscle-walls of the colon, bladder, uterus, vagina and to the blood-vessels of the pelvic viscera.

The Peripheral Ganglia.—The peripheral ganglia, as previously stated, are in more or less close relation with tissues and organs in different regions of the body. Among the members of this group may be mentioned the ciliary or ophthalmic, the sphenopalatine, the otic and the submaxillary ganglia; the ganglia in the walls of the heart, in the walls of the respiratory organs, in the walls of the stomach, and intestines and the ganglia at the base of the bladder (the pelvic ganglia).

The ganglia situated in the head are usually described in connection with and as constituent parts of the cranial nerve system. They, however, bear the same relation to the cranial that the vertebral and pre-vertebral ganglia bear to the spinal nerves. They consist of ganglion cells *from* which post-ganglionic fibers pass to glands, blood-vessels, and viscera. Motor and sensory nerves pass through one or more ganglia, though they have no anatomic connection with them. In their structure, distribution and functions they closely resemble the collateral ganglia.

1. The *ciliary* or *ophthalmic ganglion* is situated in the orbital cavity posterior to the eyeball. It is small in size, gray in color, and consists of a connective-tissue stroma containing nerve-cells. From these cells post-ganglionic fibers emerge which, after a short course forward, penetrate the eyeball and terminate in the circular fibers of the iris and the ciliary muscle.
2. The *spheno-palatine ganglion* is situated in the spheno-maxillary fossa. Its nerve-cells send non-medullated post-ganglionic fibers to the blood-vessels and glands of the mucous membrane of the nasal and oral regions.

3. The *otic ganglion* is situated just below the foramen ovale and internal to the third division of the fifth nerve. The cells give origin to post-ganglionic fibers which pass to the parotid gland by way of the auriculo-temporal division of the fifth nerve, and to the blood-vessels of the mucous membrane of the lower lip, cheek, and gums.

   Motor fibers from the small or motor root of the fifth nerve pass through this ganglion to the tensor tympani muscle.
4. The *submaxillary ganglion* is situated close to the corresponding gland. The post-ganglionic fibers to the blood-vessels and gland-cells.
5. The *cardiac ganglia* are situated in different regions in the walls of the heart; their visceral branches are distributed directly to the heart muscle-cells.
6. The *pelvic ganglia* are situated close to the base of the bladder; their visceral branches are distributed to the blood-vessels of the generative organs and to the muscle-walls of the bladder, rectum, etc.

From the distribution of the branches emerging from all the different groups of ganglia there is every reason to believe that they are in some way associated with *vaso-augmentor* and *vaso-inhibitor*, *viscero-augmentor* and *viscero-inhibitor*, *secreto-motor* and *secreto-inhibitor*, and *pilo-motor* phenomena.

THE ANATOMIC RELATION OF THE CENTRAL NERVE SYSTEM TO THE SYMPATHETIC GANGLIA

The central nerve system is associated anatomically and physiologically with the sympathetic ganglia through the intermediation of fine medullated nerve-fibers, the pre-ganglionic, which have their origin in nerve-cells situated in four different regions, viz.:

1. **The Mid-brain Region.**—The pre-ganglionic nerve-fibers that leave the brain in this region arise from groups of nerve-cells situated high up in the gray matter beneath the aqueduct of Sylvius just where it widens to form the cavity of the third ventricle. From this origin they enter the trunk of the oculo-motor nerve and in association with it enter the orbit cavity. In this situation these pre-ganglionic fibers leave the oculo-motor nerve and enter the ciliary or ophthalmic ganglion around the nerve-cells of which their terminal branches arborize. The gray post-ganglionic fibers arising in the gray cells of this ganglion enter the eyeball and are ultimately distributed to the sphincter muscle of the iris and to the ciliary muscle.
2. **The Bulbar Region.**—The pre-ganglionic fibers that leave the brain in this region arise from nerve-cells situated in the gray matter beneath the floor of the fourth ventricle a little above and below the calamus scriptorius. These fibers leave this region by three routes, viz.: in the trunks of (1) the *pars intermedia* or nerve of Wrisberg, (2) the glosso-pharyngeal and (3) the vagus.

   The pre-ganglionic fibers that leave by the nerve of Wrisberg enter the facial nerve and subsequently pass by way of the great superficial petrosal nerve to the spheno-palatine ganglion, and by way of the chorda tympani nerve to the submaxillary ganglion, around the nerve-cells of which their terminal branches arborize. The gray post-ganglionic fibers which arise in the cells of these ganglia are distributed to the blood-vessels and glands of the nose and mouth and to the blood-vessels and epithelium of the submaxillary and sublingual glands respectively.

The pre-ganglionic fibers that leave by way of the glosso-pharyngeal nerve pass into the tympanic branch or nerve of Jacobson and ultimately arborize around the cells of the otic ganglion. The gray post-ganglionic fibers which arise in the cells of this ganglion pass by way of the auriculo-temporal branch of the trigeminal nerve to the blood-vessels and epithelium of the parotid gland.

The pre-ganglionic fibers that leave in the trunk of the vagus nerve are ultimately distributed to the ganglia of the heart, stomach, small intestine, etc., around the nerve-cells of which their terminal branches arborize. The gray post-ganglionic fibers which arise in these ganglia pass to the heart-fibers, to the non-striated muscle-fibers in the walls of the stomach, intestines, etc. These fibers contained in the facial, glosso-pharyngeal and vagus nerves, together with their ganglionic continuations, have collectively been termed the *bulbar autonomic* system. Together with the fibers in the oculo-motor nerve they have been termed the *cranio-bulbar autonomic* system.

3. **The Mid-spinal Cord Region.**—The pre-ganglionic nerve-fibers that leave the spinal cord in this region arise from groups of nerve-cells situated in the gray matter between the levels of origin of the second thoracic and the second and third, perhaps the fourth, lumbar nerves. From this origin the fine pre-ganglionic fibers emerge from the cord in the ventral roots of the thoracic and upper lumbar nerves and hence naturally fall into two groups, viz.: the thoracic and the lumbar. Both groups of nerves accompany the ventral motor roots of the spinal nerves to about the point where each nerve divides into an anterior and a posterior branch; they then leave and enter the vertebral or sympathetic chain of ganglia. The branches of communication are known as the *white rami communicantes*. The nerve-fibers composing these communicating branches all terminate around the nerve-cells of the ganglia at the same and at somewhat different levels and in different regions.

The *thoracic* pre-ganglionic fibers in accordance with their distribution may be divided into five groups, viz.:

(*a*) Those fibers which emerge from the spinal cord in each of the thoracic nerves and which terminate around the cells of the ganglia at the same level.

(*b*) Those fibers which emerge from the spinal cord in the thoracic nerves from the fourth to the tenth and which after entering the vertebral chain turn upward and finally terminate around the cells of the first thoracic or stellate ganglion.

(*c*) Those fibers which emerge from the cord in the second and third thoracic nerves and which after entering the vertebral chain turn upward and terminate around the cells of the inferior cervical ganglion.

(*d*) Those fibers which emerge from the cord in the second, third and perhaps the fourth thoracic nerves and which, after entering the vertebral chain turn upward and pass through the various ganglia and cord and finally terminate around the cells of the superior cervical ganglion.

(*e*) Those fibers which emerge from the spinal cord in the thoracic nerves from the fifth to the tenth and which after entering the vertebral chain pass across it and turn downward and forward uniting at different levels to form the *greater* and *lesser splanchnic* nerves, the terminal branches of which arborize around the cells of the semilunar, the renal, and the superior mesenteric ganglia.

The *lumbar* pre-ganglionic fibers in accordance with their distribution may be divided into three groups, viz.:

(*a*) Those fibers which, after pursuing a similar course to the preceding terminate around the cells of the ganglia at the same level.

(*b*) Those fibers which after entering, cross the vertebral chain and then pass forward as the *inferior splanchnic* nerves to terminate around the cells of the inferior mesenteric ganglion.

(*c*) Those fibers which after entering, descend the vertebral chain to terminate around the cells of the successive ganglia as far as the third sacral. It is probable that some fibers from the lower thoracic nerves also descend the lumbar chain.

By reason of this anatomic distribution, the thoracico-lumbar pre-ganglionic fibers become related to all the vertebral and the pre-vertebral ganglia. From these various ganglia, as stated on page 645 post-ganglionic fibers arise which either as gray rami communicantes enter the spinal nerves or as rami viscerales pass direct to their termination. In either case the nerve-fibers ultimately become histologically and physiologically related to non-striated vascular and visceral muscle-fibers and to epithelium of glands. The specific distributions of the post-ganglionic fibers are stated in the paragraphs relating to the ganglia themselves. A connection is thus established between the cells of the spinal cord and the motor tissues by means of the pre- and post-ganglionic nerve-fibers. These nerves include, therefore, all the vaso-motor (constrictor) nerves, the secreto-motor nerves for the sweat glands, the thyroid and the adrenal glands, and a large part of the viscero-motor (inhibitor) nerves.

The thoracico-lumbar pre-ganglionic nerves together with their post-ganglionic continuations together constitute the *thoracico-lumbar autonomic nerve* system.

4. **The Sacral Spinal-cord Region.**—The pre-ganglionic nerve-fibers that leave the spinal cord in this region arise from groups of nerve-cells situated in the gray matter between and including the levels of origin of the second, the third and the fourth (?) sacral nerves. From this origin the pre-ganglionic fibers emerge from the cord in association with the large motor fibers composing the ventral roots of these sacral nerves and pass with them to the interior of the pelvis. Here they leave the sacral nerves and enter the pudendal or pelvic nerve (the nervus erigens) and finally terminate around the cells of the pelvic ganglia. From these ganglia post-ganglionic fibers arise which pass onward to be distributed to the non-striated muscle-fibers of pelvic viscera and the blood-vessels of the external generative organs. These fibers contained in the sacral nerves together with their post-ganglionic continuation have collectively been termed the *sacral autonomic* system. It may be regarded as a

special nerve system for the anal end of the gut and structures developmentally connected with it.

From the distribution of the pre-ganglionic fibers and their histologic connection with the sympathetic ganglia and from the distribution and histologic connection of the branching fibers from the ganglia there is every reason to believe that the autonomic nerve system includes all the vaso-motor, some of the vaso-inhibitor, the viscero-motor and the viscero-inhibitor, the secreto-motor and the secreto-inhibitor nerves.

Structure of the Interconnecting Cords.—The interconnecting cords are composed of non-medullated and medullated nerve-fibers. The former are the axons of cells found in the ganglia more centrally located; the latter are derived from the spinal nerves, from the fibers of which, however, they differ in character, being much smaller and finer. The fibers of the interconnecting cords, as a rule, transmit nerve impulses from the more centrally to the more peripherally located ganglia, and are, therefore, termed *rami efferentes*. In the vertebral chain some of the cords transmit nerve impulses upward, others downward, others again forward, to the pre-vertebral and peripheral ganglia.

Among the rami efferentes or interconnecting cords, there are some which possess special interest for the physiologist, viz.:

1. The *cervical* which connects the thoracic ganglia with the superior cervical ganglion. It is composed mainly of pre-ganglionic medullated fibers derived originally from the thoracic spinal cord.
2. The *great splanchnic* nerve formed mainly by the union of pre-ganglionic fibers which cross the vertebral chain in the region of the fifth to the tenth thoracic ganglia. It connects the cells of the spinal cord with the cells of the semilunar ganglion.
3. The *small splanchnic* nerve formed by the union of pre-ganglionic medullated fibers that cross the vertebral chain in the region of the ninth and tenth thoracic ganglia. It connects the cells in the spinal cord with the renal and perhaps the superior mesenteric ganglion.
4. The *inferior splanchnic* nerves formed by the union of pre-ganglionic medullated fibers that cross the upper lumbar chain in the region of the second and third lumbar ganglia. They connect the cells in the spinal cord with the inferior mesenteric ganglion.

Afferent Sympathetic Fibers.—With the foregoing groups of pre-ganglionic autonomic fibers in the thoracic and lumbar regions there is associated a certain number of afferent fibers which impart a certain degree of sensibility to the organs of the thoracic and abdominal regions. Though these organs in the physiologic condition do not appear to be endowed with much sensibility, nevertheless, in pathologic conditions they become exceedingly sensitive and give rise to extremely painful sensations. The afferent nerves which mediate these sensations have their origin in nerve-cells located in the ganglia of the dorsal roots of the spinal nerves; from this origin they pass outward by way of the white rami into nerve trunks which pass to the organs in the thoracic and abdominal cavities, *e.g.*, the cardiac plexus and the splanchnic nerves and the sacral nerves to the pelvic organs. The presence of afferent nerves in the splanchnics can be shown by stimulating the central end or even the white rami with electric currents, a procedure that gives rise to pain as well as a reflex rise of blood-pressure. The number of afferent nerve-fibers in any of the these nerve trunks is quite small in comparison with the efferent fibers. In pathologic conditions of the organs the sensations to which they give rise are frequently referred to areas of the cutaneous surface overlying the lesion.

THE FUNCTIONS OF THE AUTONOMIC NERVE SYSTEM

The view according to which the sympathetic ganglia are to be regarded as independent organs endowed with functions of their own and in nowise directly dependent for their activities on the central nerve system is at the present very largely discarded. Peripheral structures cease to exhibit their characteristic functions after division of the spinal nerves in connection with their related ganglia. This does not exclude the possibility of the sympathetic cell-body, in virtue of the interchanges between it and the blood and lymph by which it is surrounded, maintaining its own nutrition and exerting possibly a favorable influence over the nutrition of peripheral tissues to which its post-ganglionic branches are distributed.

From the number and fineness of the ultimate terminations of the branches given off from the ganglion cells as well as their extensive distribution in all regions of the body, it has been suggested that they are distributors of the nerve impulses discharged in consequence of the stimulating influence of nerve impulses coming from the spinal cord, through the pre-ganglionic fibers.

From the distribution of the post-ganglionic fibers, viz.: to the walls of the blood-vessels, to the walls of the viscera, and to the epithelium of glands and in some animals to the muscles of the hair follicles, it may be inferred that the ganglia are associated with vaso-motor, viscero-motor, secreto-motor and pilo-motor phenomena; and since the pre-ganglionic fibers are always associated with the ganglia, anatomically and physiologically, it can be said that they too are associated with the same series of phenomena.

The functions of the autonomic nerve system, as determined from its anatomic distribution and the results of experimental investigations, are to *augment* or to *inhibit* the tonus of the blood-vessels including the heart, the tonus of visceral walls and the activity of the epithelium of glands, and are, therefore, the sum total of the functions of the vaso-motor, viscero-motor and secreto-motor nerves, that is, the nerves which collectively constitute this system. The extent to which these different modes of activity manifest themselves in one or more regions of the body will depend to some extent on the strength of the stimulus and the portion of the system subjected to experiment, as will be apparent from the following statements.

The Functions of the Mid-brain Autonomic Nerves.—The functions of the efferent pre-ganglionic nerve-fibers contained in the trunk of the oculomotor nerve, together with their post-ganglionic continuations (the ciliary ganglion and its branches), are (*a*) To *augment* the tonus or degree of contraction of the *sphincter pupillæ* or the *sphincter iridis* in accordance with increasing intensities of light, and (*b*) to *augment* the tonus or degree of contraction of the ciliary muscle accompanying efforts of accommodation. The result of the contraction of the sphincter pupillæ is a diminution in the diameter of the pupil and hence a diminution in the amount of light entering the eye so that the perception of the image may be sharp and distinct. The result of the contraction of the ciliary muscle is a relaxation of the suspensory ligament of the lens whereupon the latter becomes more convex on its anterior surface, and hence adjusted for near vision. These and similar facts are shown by stimulation and division of these nerves either pre- or post-ganglionic with induced electric currents.

The Functions of the Bulbar Autonomic Nerves.—The efferent pre-ganglionic nerve-fibers contained primarily in the nerve of Wrisberg or *pars intermedia*, and secondarily in the facial nerve may be divided into two groups, viz.: (*a*) those passing by way of the great petrosal nerve to the spheno-palatine ganglion, and (*b*) those passing by way of the chorda-tympani nerve to the submaxillary and sublingual ganglia. The functions of the great petrosal fibers together with their post-ganglionic continuations (the spheno-palatine ganglion and its branches) are (*a*) To *inhibit* the contraction of the blood-vessels of the mucous membrane of the nose, soft palate, upper part of the pharynx, the roof of the mouth and upper lip, and (*b*) to *augment* the secretion of the mucous glands of the corresponding region. The functions of the chorda-tympani fibers and their ganglionic continuations (the submaxillary and sublingual ganglia and their branches) are (*a*) To *inhibit* the tonus of the blood-vessels of the submaxillary and sublingual glands and (*b*) to *augment* the activities of their epithelium and thus increase their secretions.

The function of the efferent pre-ganglionic fibers contained in the trunk of the glosso-pharyngeal nerve together with their post-ganglionic continuations (the otic ganglion and its branches) are (*a*) To *inhibit* the contraction of the blood-vessels of the parotid gland and (*b*) to *augment* the activities of its epithelium and thus increase its secretion.

The efferent pre-ganglionic nerve-fibers contained in the trunk of the vagus nerve together with their post-ganglionic continuations are as follows: (*a*) To *inhibit* the tonus and contractile power of the heart-muscle; (*b*) to *inhibit* and sometimes *augment* the contraction of the *esophagus* and of the *sphincter cardiæ*; (*c*) to *inhibit* the tonus of the cardiac end of the stomach for the purpose of receiving incoming amounts of food; (*d*) to *augment* the tonus and the contractile power of the gastric musculature and the pyloric sphincter; (*e*) to *augment* and sometimes *inhibit* the tonus of the bronchial musculature; (*f*) to *inhibit* the sphincter muscle of the common bile duct and to *augment* the tonus and contractile power of the visceral muscles in the walls of the gall-bladder; (*g*) to *augment* the tonus and contractile power of the visceral muscles of the walls of the small intestine, and (*h*) to *augment* and sometimes to *inhibit* the activities of the epithelium of the gastric and pancreatic glands and thus increase their secretions. These various phenomena result when these various efferent nerves are divided and their peripheral extremities are appropriately stimulated.

The Functions of the Thoracic and Lumbar Autonomic Nerves.—The efferent pre-ganglionic nerve-fibers that leave the spinal cord in the ventral roots of the thoracic and upper lumbar nerves together with their post-ganglionic continuations, have been shown by experiment to be vaso-motor (constrictor), secreto-motor, viscero-motor and in some animals pilo-motor in functions. The origin, course and distribution of these nerve-fibers have been stated on pages 377 and 473. The specific functions of these fibers will depend on the regions of the body to which they are distributed (See page 648.)

The functions of the thoracic fibers that terminate in the ganglia of the same levels are (*a*) to *augment* the tonus and the degree of the contraction of the blood-vessels of the skin of the arm and trunk of the body; and (*b*) to *augment* the activities of the epithelium of the sweat-glands in the corresponding regions. Stimulation of either the pre- or post-ganglionic fibers produces the foregoing phenomena.

The functions of the fibers that ascend the sympathetic chain to terminate in the first thoracic, the inferior cervical ganglia are (*a*) to accelerate the rate and the force of the contraction of the heart-muscle, and (*b*) perhaps *augment* the activities of the epithelium of the thyroid gland. The pre-ganglionic-fibers having these important functions emerge from the spinal cord for the most part in the ventral roots of the second and third thoracic nerves. After leaving these nerves by way of the *rami communicantes* they enter the thoracic chain and pass upward to terminate in and around the cells of the inferior cervical ganglion in man and in the first thoracic ganglion in certain other mammals. The post-ganglionic visceral fibers—the cardiac nerves—that arise in the cells of these ganglia pass downward and forward and reach the heart by way of the cardiac plexus. Stimulation of these nerves causes the same effects in the heart as stimulation of the pre-ganglionic fibers in any part of their course. The center of origin of these accelerator and augmentor cardiac fibers has not been definitely located but there are reasons for thinking it is in the medulla oblongata.

The functions of the fibers which in their upward course form the cervical cord and finally terminate around the nerve cells of the superior cervical ganglion are:

(*a*) To *augment* the tonus and increase the contraction of the blood-vessels of the skin and mucous membrane of different portions of the head, face and neck; (*b*) to *augment* the contraction of the blood-vessels of the submaxillary, the sublingual and the parotid glands; and (*c*) to *augment* the activity of the epithelium of the sweat glands of the head, face and neck, and possibly of the salivary glands as well. (*e*) To *augment* the tonus and the contractions of the *dilatator pupillæ* muscle, thus antagonizing and overcoming the contraction of *sphincter pupillæ* muscle and establishing a dilatation of the pupil.

The foregoing effects may be demonstrated by exposing and dividing the cervical cord and then stimulating the peripheral end. The same phenomena follow stimulation of the post-ganglionic branches. That the superior cervical ganglion, like ganglia elsewhere in the body, is the cell station between the spinal cord and the peripheral organs is shown by the fact discovered and applied by Langley that the intra-venous injection of nicotin or the local application of it to the ganglion itself, impairs the conductivity of the terminals of pre-ganglionic fibers, after which their stimulation has no effect on the ganglion cells, though the latter retain their activity, as shown on direct stimulation.

The functions of the fibers that cross the sympathetic chain and unite to form the greater and lesser splanchnic nerves together with their ganglionic continuations (semilunar ganglion and the fibers of the solar plexus) are: (*a*) To *augment* the tonus and contractile power of the walls of the blood-vessels of the stomach and intestines as far as the descending colon (the so-called splanchnic vascular area) and the blood-vessels of the kidney and spleen; and (*b*) to *inhibit* the tonus and diminish the degree of contraction of the muscle walls of the stomach and intestine; (*c*) to *inhibit* the tonus, during digestion, of the sphincter muscle of the common bile duct; and (*d*) to *augment* the tonus and degree of contraction of the muscle-walls of the gall-bladder; (*e*) to *augment* the tonus of the ileo-colic sphincter muscle; (*f*) to *augment* the secretion of the adrenal bodies.

These effects are readily observed if the great splanchnic nerve is first divided and then its peripheral end stimulated with induced electric currents. With the division of the nerve the blood-vessels of the splanchnic area, as well as of neighboring organs, dilate, attended by a sudden fall of the general blood-pressure; with the beginning of the stimulation the blood-vessels of the corresponding areas at once contract, coincidently with which there is a rapid rise in the general blood-pressure.[1] The division of the splanchnics is followed by a rise in the tonus of the muscle-walls of the intestine (due to the augmentor activity of the now unopposed vagi nerves); stimulation of the peripheral end of the splanchnics is followed by a marked inhibition of the tonus.

The functions of the *lumbar* fibers that terminate in the ganglia of the same levels are: (*a*) To *augment* the tonus and the degree of contraction of the blood-vessels of the skin of the trunk to which they are distributed; and (*b*) to *augment* the activities of the sweat-glands of the corresponding regions.

The functions of the nerve-fibers that cross the sympathetic chain and unite to form the *inferior splanchnic* nerves, together with their ganglionic continuations (the inferior mesenteric ganglion and the hypogastric plexus), are: (*a*) To *augment* the tonus and the contractile power of the blood-vessels of the pelvic viscera; (*b*) to *inhibit* the tonus and diminish the contractile power of the muscle-walls of the large intestine; (*c*) to *augment* the tonus of the sphincter muscle of the urinary bladder, and to *inhibit* the tonus of the muscle-walls of the bladder during the intervals of urination; (*d*) to *augment* the tonus and contractile power of the uterus.

These various phenomena arise when either the pre-ganglionic or the post-ganglionic fibers in the hypogastric plexus are stimulated with induced electric currents.

The functions of the fibers which descend the sympathetic chain to terminate around the cells of the lumbar and sacral ganglia are (*a*) to *augment* the tonus and the degree of contraction of the blood-vessels of the skin of the hip and leg; and (*b*) to *augment* the activities of the epithelium of the sweat-glands of the corresponding parts. By reason of the distribution of the visceral branches of the sacral ganglia a similar contraction of the blood-vessels is observed in portions of the pelvic viscera and the external genitalia.

The Functions of the Sacral Autonomic Nerves.—The functions of the pre-ganglionic nerve-fibers that leave the spinal cord by way of the ventral roots of the second, third and perhaps the fourth sacral nerves, together with their post-ganglionic continuations (the pelvic ganglia and their branches) are: (*a*) To *inhibit* the tonus and cause a dilatation of the blood-vessels of the generative organs; (*b*) to *inhibit* the tonus of the sphincter muscle of the bladder; (*c*) to *augment* the contraction of the detrusor muscle during urination; (*d*) to *augment* the tonus and contractile power of the muscle-walls of the colon and rectum, and the rectal sphincters.

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[1] Occasionally stimulation of the splanchnic is followed by a slight primary inhibition and dilatation of the blood-vessels which would lead to the inference that vaso-dilatator fibers are also present; these fibers, however, do not belong properly to the autonomic system as their center of origin is in the ganglia of the dorsal roots of the spinal nerves. (See pages 380.)

Summary.—The autonomic system consists of:

1. The autonomic tissues, viz.: the non-striated, visceral and vascular muscle tissue, cardiac striated muscle tissue and epithelial tissue.
2. The autonomic nerves.

The autonomic nerves consist of two successively arranged neurons. The first has its origin in cells of the central nerve system; the second has its origin in cells of the sympathetic ganglia. The former is termed pre-ganglionic, the latter post-ganglionic. The pre-ganglionic neuron arborizes peripherally around the cells of the sympathetic ganglia; the post-ganglionic terminates by fine branchings around the cells of the tissues.

The pre-ganglionic neurons have their origin in four separate regions of the central nerve system, viz.: (1) The mid-brain region; (2) the medulla oblongata; (3) the mid-spinal cord region and (4) the sacral region.

The autonomic system of nerves as evident from their distribution comprises:

1. The *viscero-augmentor* and *viscero-inhibitor* nerves for the non-striated muscles of the eyeball (iris and ciliary muscle) of the lower portion of the esophagus, of the trachea and bronchial tubes, of the stomach, of the small and large intestine, the gall-bladder and the pelvic organs.
2. The *vaso-dilatator* nerves for the non-striated muscles of the blood-vessels of the salivary glands, the mucous and serous glands of the nose, mouth and pharynx, and of the genital organs.
3. The *vaso-constrictor* nerves for the non-striated muscles of the blood-vessels of the skin of the head, face, neck, trunk, arms, and legs, alimentary canal, liver, spleen, kidney, adrenals and genital organs.
4. The *cardio-augmentor* and *cardio-inhibitor* nerves for the heart.
5. The *secreto-augmentor* and *secreto-inhibitor* nerves for the epithelial tissue of the salivary glands, of the mucous and serous glands of the mouth, nose, and pharynx, of the trachea and bronchial tubes, of the gastric glands, of the thyroid, of the pancreas, of the adrenals, of the liver, and the sweat-glands of the skin of the head, face, neck, trunk, arms, legs and of the glands in connection with the genital organs.

The centers of origin of the autonomic nerves possess a certain degree of tonus, maintained in all probability by changes of a chemic character, between the constituents of the nerve cells and the constituents of the blood by which they are surrounded. In consequence of this tonus, they maintain a certain degree of activity in the tissues to which the autonomic fibers are distributed. Given this tonus the autonomic centers may be excited tc increased activity: (1) By nerve impulses transmitted by afferent nerves from the surfaces of the body; and (2) by nerve impulses descending from the cerebrum in consequence of psychic states of an affective or emotional character.

The nature and strength of the stimulus applied to the surface of the body, and the nature and intensity of the affective or emotional state will naturally determine the degree and extent of the resulting activity of the autonomic tissues.

NOTE.—Langley to whom we are so largely indebted for the present state of our knowledge of the anatomy and physiologic relations, not only of different portions of this system, but of the system in its entirety, introduced the term "autonomic," on account of the insufficiency of the older nomenclature, *e.g.*, "sympathetic," "ganglionic," "vegetative," "organic," "visceral," etc., to fully express its anatomic relations and physiologic action. By this term it is implied that this system is independent in action; that is, independent of volitional control, that its activity is determined by nerve impulses coming from the periphery, though subject to modifications by cerebral states of an affective or emotional character. Thus he states (Journal of Physiology, vol. 23) "I propose to substitute the word autonomic " * * *; "the autonomic nervous system means the nervous system of the glands and of the involuntary muscle." "I propose the term autonomic nervous system for the sympathetic system and the allied nervous systems of the cranial and sarcal nerves and for the local nervous system of the gut " * * *. "I conclude that there is no fundamental difference between the pre-ganglionic fibers of the body, whether they belong to the cranial, the sympathetic or the sacral autonomic systems." "The word autonomic nervous system consists of the sympathetic system, of the cranial autonomic system, and the enteric system, the plexuses of Auerbach and Meissner."

Gottlieb and Meyer, partly on the basis of the difference in the physiologic action of certain drugs on different portions of this system, and partly on the apparent antagonism in the action of the nerves which arise from the bulbar and sacral region of the spinal cord, to those which arise from the thoracic and upper lumbar regions, proposed a modification of the terminology. Thus they applied to the entire system the term "vegetative," but at the same time retained the term autonomic for the fine medullated pre-ganglionic fibers in the cranio-bulbar and in the sacral nerves, *i.e.*, those nerves not in physiologic relation with the chain of sympathetic ganglia, though related to peripheral ganglia. The pre-ganglionic cranio-bulbar and sacral nerve-fibers together with their post-ganglionic continuations innervate the anterior and posterior ends of the digestive tract and associated structures respectively, while the pre-ganglionic thoracico-lumbar nerve-fibers and their ganglionic continuations innervate the sweat-glands and blood-vessels of the head, face, extremities and the body-walls and the blood-vessels and muscle-walls of the abdominal viscera. Associated with these latter nerves are the efferent fibers of the vagus which innervate the heart, the blood-vessels and glands of the viscera of the thorax and part of the abdomen as well.

By reason of the double innervation of various organs of the body and the opposite effects produced by stimulation on the one hand of the autonomic cranio-bulbar and sacral nerve-fibers and on the other hand of the pre- and post-ganglionic fibers of the thoracico-lumbar nerves, Gottlieb and Meyer concluded, that there is a fundamental difference in the functions of the cranio-bulbar and sacral regions and the thoracico-lumbar regions of the spinal cord. This antagonism is shown by the effects observed in the iris and in the action of the heart by alternate stimulation of the cranio-bulbar and thoracic fibers which are distributed to these structures. It should be borne in mind, however, that even though pre-ganglionic fibers leave the spinal cord by way of the thoracic nerves, the nerve-cells from which they arise may lie in other and even distant regions. Thus it is well known that the vaso-motor center which through thoracic nerves constricts the blood-vessels of the salivary glands, the mucous glands of the mouth and nose lies high up the bulbar region, not far from the vaso-dilatator center, which through bulbar fibers (in the chorda tympani and glosso-pharyngeal) supplies and dilates the same blood-vessels of the corresponding structures. It is also believed that the dilatator pupillæ or iridis center which, through nerve-fibers that leave the spinal cord through the second thoracic nerve and then pass upward in the sympathetic chain to the superior cervical ganglion and thence to the dilatator fibers of the iris, is also located near the group of nerve-cells which gives origin to the nerve-fibers for the sphincter muscle of the iris. It is also believed that the accelerator nerves for the heart which emerge from the spinal cord in the second and third thoracic nerves come from a center lying in the bulbar region not far from the center from which the inhibitor fibers in the vagus come.

Nevertheless there are other instances in which this antagonism does exist, *e.g.*, in the effects of the efferent fibers of the vagus and the splanchnic nerves on the muscle-wall of the intestine, the former augmenting, the latter inhibiting the contraction and so in other regions. But this does not necessitate the employment of new terms. It suffices to say that there is a difference in the action of different parts of the general autonomic system. It is just as probable, however, that the difference in the effects observed following stimulation of the two classes of nerves depends on the character of their peripheral terminations rather than on a difference in the character of the central cells.

Huber, in a recent review of the morphology of the sympathetic system, says in regard to the foregoing division, "such a division of the autonomic nerve system does not seem justifiable when viewed in the light of a morphologic study of the ganglia with their constituent neurons, the terminations of the neuraxis of the neurones in the various tissues, and the connections of these neurones with the cerebrospinal axis by means of the pre-ganglionic fibers; morphologically considered, the entire autonomic system is a unit and will be treated as such. The minor structural differences, more apparent than real, observed in the neurons of certain of the cranial autonomic ganglia and in the entire system, do not warrant, it would seem to me, a regional subdivision of the autonomic system, when considered from the viewpoint of structure."

CHAPTER XXVII

PHONATION; ARTICULATE SPEECH

Phonation, the emission of vocal sounds, is accomplished by the vibration of two elastic membranes which cross the lumen of the larynx anteroposteriorly and which are thrown into vibration by a blast of air from the lungs.

Articulate speech is a modification of the vocal sounds or the voice produced by the teeth and the muscles of the lips and tongue and is employed for the expression of ideas.

The larynx, the organ of the voice, is situated in the fore part of the neck, occupying the space between the hyoid bone and the upper extremity of the trachea. In this situation it communicates with the cavity of the pharynx above and the cavity of the trachea below. From its anatomic relations and its internal structure—the interpolation of the elastic membranes—the larynx subserves the two widely different yet related functions, respiration and phonation.

THE ANATOMY OF THE LARYNX

The larynx consists primarily of a series of cartilages united one with another in such a manner as to form a more or less rigid framework, yet possessing at its different joints, a certain amount of motion; and secondarily, of muscles and nerves which conjointly impart to the cartilages the degree of movement necessary to the performance of the laryngeal functions. It is covered externally by fibrous tissue and lined throughout by mucous membrane continuous with that lining the pharynx and trachea.

The larynx presents a superior or pharyngeal and an inferior or tracheal opening. The pharyngeal opening is triangular in shape, the base being directed forward, the apex backward. The plane of this opening in the living subject is almost vertical. The tracheal opening is circular in shape and corresponds in size with the upper ring of the trachea. Viewed from above, the general cavity of the larynx is seen to be partially subdivided by two membranous bands—the *vocal bands* or cords—which run from before backward in a horizontal plane. The space between the bands, the *glottis*, varies in size and shape from moment to moment in accordance with respiratory and phonatory necessities. The average width of the glottis, at its widest part, during quiet respiration is about 13.5 mm. in men and 11.5 mm. in women. With the advent of phonation the vocal membranes are at once approximated, and to such an extent that the glottic opening is reduced to a mere slit. It is then spoken of as the *rima glottidis*, or chink of the glottis.

The space above the vocal bands, the supra-glottic or supra-rimal space, is triangular in shape and extends from the pharyngeal opening to the plane of the vocal bands. The mucous membrane lining the walls of this space, presents on either side, just above the vocal bands, a crescentic fold which runs from before backward, and is known as the false vocal band or cord. Between the true and false bands there is a cavity or space prolonged upward and outward for some distance, forming what is known as the ventricle of the larynx. The space below the vocal bands, the infra-glottic or infra-rimal space, is narrow above and elongated from before backward, but wide and circular below, corresponding to the lumen of the trachea. (Fig. 273.)

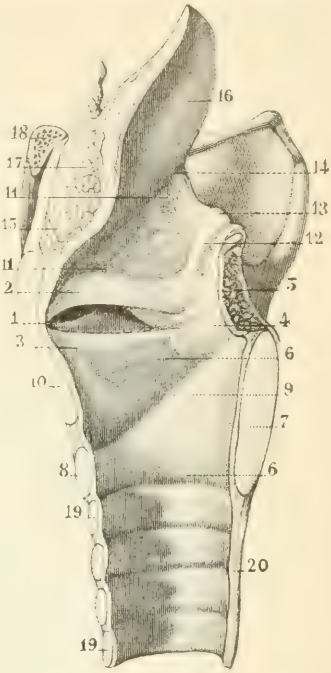

Fig. 273.—Longitudinal Section of the Human Larynx, Showing the Vocal Bands. 1. Ventricle of the larynx. 2. Superior vocal cord. 3. Inferior vocal cord. 4. Arytenoid cartilage. 5. Section of the arytenoid muscle. 6, 6. Inferior portion of the cavity of the larynx. 7. Section of the posterior portion of the cricoid cartilage. 8. Section of the anterior portion of the cricoid cartilage. 9. Superior border of the cricoid cartilage. 10. Section of the thyroid cartilage. 11, 11. Superior portion of the cavity of the larynx. 12, 13. Arytenoid gland. 14, 16. Epiglottis. 15, 17. Adipose tissue. 18. Section of the hyoid bone. 19, 19, 20. Trachea.—(*Sappey.*)

The Laryngeal Cartilages, Articulations, and Ligaments.—The cartilages which compose the framework of the larynx are nine in number, three of which are single: viz., the cricoid, the thyroid, and the epiglottis, while six occur in pairs: viz., the arytenoids, the cornicula laryngis, and the cuneiform. (Figs. 274 and 275.)

The *cricoid* cartilage is the foundation cartilage, and affords support to the remaining cartilages and the structures attached to them. In shape it resembles a signet-ring, the broad quadrate portion of which is directed backward, while the narrow circular portion is directed forward. It rests upon the upper ring of the trachea, to which it is firmly attached by fibrous tissue. The posterior upper border of the quadrate portion presents on either side an oval convex facet for articulation with the arytenoid cartilage. The long axis of this facet is directed downward, outward, and forward.

The *thyroid*, the largest of the laryngeal cartilages, is composed of two flat quadrilateral plates, united anteriorly at an angle of about 90 degrees. Each plate is directed backward and outward and terminates in a free border, which is prolonged upward and downward for some distance, terminating in two processes, the superior and inferior cornua. The upper border to the thyroid is deeply notched in front. The inferior border overlaps laterally the cricoid.

The *epiglottis* is a leaf-shaped piece of cartilage attached to the thyroid at the median notch. It is firmly united by membranes and ligaments to the thyroid and arytenoid cartilages and to the base of the tongue.

The *arytenoid cartilages* are two in number and symmetric in shape. Each cartilage is a triangular pyramid, the apex of which is recurved, and directed backward and inward. The base presents three angles—an anterior, an external, and an internal. The anterior angle is long and pointed and projects forward in a horizontal plane. It serves for the attachment of the vocal membranes and is, therefore, termed the *vocal process*. The external angle is short, rounded, and prominent, and serves for the attachment of muscles. The internal angle affords a point of insertion for a ligament. The inferior surface of the arytenoid is concave for articulation with the convex surface of the cricoid facet. Its long axis, however, is directed from before backward and almost at right angles to the long axis of the cricoid facet.

The *cornicula laryngis* and the *cuneiform* cartilages are small nodules of yellow elastic cartilage embedded in a fold of membrane which unites the arytenoid and the epiglottis. They are fragments of a ring of cartilage which in some animals—*e.g.*, ant-eater—extends between these two cartilages.

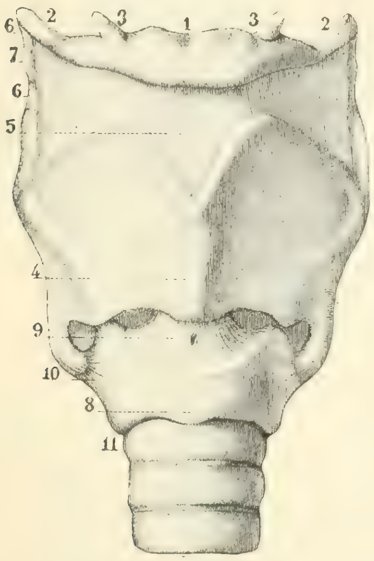

FIG. 274.

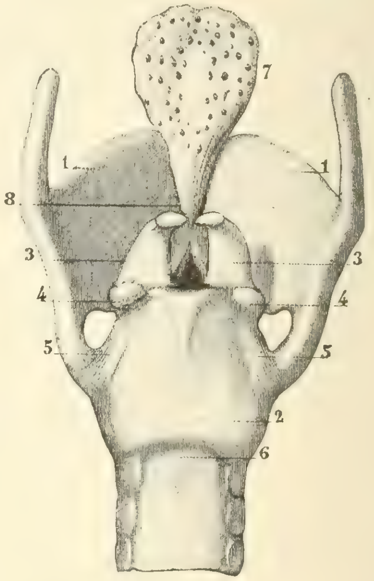

FIG. 275.

FIG. 274.—LARYNGEAL CARTILAGES AND LIGAMENTS, ANTERIOR SURFACE. 1. Hyoid bone. 2, 2, 3, 3. Greater and lesser cornua. 4. *Thyroid cartilage.* 5. *Thyro-hyoid membrane.* 6. Thyro-hyoid ligaments. 7. Cartilaginous nodule. 8. *Cricoid cartilage.* 9. The *crico-thyroid membrane.* 10. The crico-thyroid ligaments. 11. Trachea.—(*Sappey.*)

FIG. 275.—LARYNGEAL CARTILAGES AND LIGAMENTS, POSTERIOR SURFACE. 1, 1. *Thyroid cartilage.* 2. *Cricoid cartilage.* 3, 3. *Arytenoid cartilages.* 4, 4. *Crico-arytenoid articulations.* 5, 5. *Crico-thyroid articulations.* 6. Union of the cricoid cartilage and of the trachea. 7. Epiglottis. 8. Ligament uniting it to the reëntering angle of the thyroid cartilage.—(*Sappey.*)

The *crico-thyroid articulation* is formed by the opposition of the tip of the inferior cornu of the thyroid cartilage and an articular facet on the side of the cricoid. The joint is provided with a synovial membrane and enclosed by a capsular ligament. The movements permitted at this joint take place around a horizontal axis and consist of an upward and downward movement of both the thyroid and cricoid, combined with a sliding movement of the latter upward and backward.

The *crico-arytenoid articulation* is formed by the apposition of the articulating sufaces of the cricoid and arytenoid cartilages. This joint is provided with a synovial membrane and enclosed by a loose capsular ligament which would permit of an extensive sliding of the arytenoid cartilage downward and outward were it not prevented by the posterior crico-arytenoid ligament, which is attached, on the one hand, to the cricoid, and, on the other, to the inner angle of the arytenoid. The movements permitted at this joint are: (1) Rotation of the arytenoid around a vertical axis which lies close to its inner surface. (2) A sliding motion inward and forward with inward rotation of the vocal process, or a sliding motion outward and backward with outward rotation of the vocal process. In either case the process describes an arc of a circle. (3) A sliding movement toward the median line in consequence of which the inner surfaces of the arytenoids are brought almost in contact.

The *crico-thyroid membrane* is composed mainly of elastic tissue. It may be divided into a mesial and two lateral portions. The mesial portion is well developed, triangular in shape, and unites the contiguous borders of the cricoid and thyroid cartilages. The lateral portion is attached below to the superior border of the cricoid. From this attachment it passes upward and inward under cover of the thyroid. As it ascends it elongates and becomes thinner, and is finally attached anteriorly to the thyroid near the median line, and posteriorly to the vocal process of the arytenoid, thus constituting the *inferior thyro-arytenoid* ligament. It is covered internally by mucous membrane and externally by the internal thyro-arytenoid muscle. The free edge of this ligament forms the basis of the true vocal band. A superior thyro-arytenoid ligament forms the basis of the false vocal band.

The *thyro-hyoid* membrane, composed of elastic tissue, unites the superior border of the thyroid to the hyoid bone.

The *mucous membrane* lining the larynx is thin and pale. As it passes downward it is reflected over the superior thyro-arytenoid ligament, and assists in the formation of the false vocal band; it then passes into and lines the ventricle, after which it is reflected inward over the superior border of the thyro-arytenoid muscle and ligament, and assists in the formation of the true vocal band; it then returns upon itself and passes downward over the lateral portion of the crico-thyroid membrane into the trachea.

The Vocal Bands.—The thin, free, reduplicated edge of the mucous membrane constitutes the true vocal band. The surface of the mucous membrane is covered by ciliated epithelium except in the immediate neighborhood of the vocal bands.

The vocal bands are attached anteriorly to the thyroid cartilage near the receding angle and posteriorly to the vocal processes of the arytenoid cartilages. They vary in length in the male from 20 to 25 mm. and in the female from 15 to 20 mm.

The Muscles of the Larynx.—The muscles which have a direct action on the cartilages of the larynx and determine the position of the vocal bands both for respiratory and phonatory purposes, and which regulate their tension as well, are nine in number and take their names from their points of origin and insertion: viz., two posterior crico-arytenoids, two lateral crico-arytenoids, two thyro-arytenoids, one arytenoid, and two crico-thyroids (Figs. 276 and 277).

The *posterior crico-arytenoid* muscle lies on the posterior surface of the quadrate plate of the cricoid cartilage, on either side of the median line, from which it takes its origin. The fibers of the muscle pass upward and outward and in their course converge to be inserted into the external angle of the arytenoid cartilage. The superior and more horizontally directed fibers rotate the arytenoid around its vertical axis; the inferior and obliquely directed fibers draw the cartilage downward and inward. As a result of the action of the muscle in its entirety, the vocal process is turned upward and outward, and as the vocal band is carried with it the glottis is widened, a condition necessary to the free entrance of air into the lungs (Fig. 278). Since the contraction of the crico-arytenoid has this result, it is generally spoken of as the *abductor* or *respiratory* muscle.

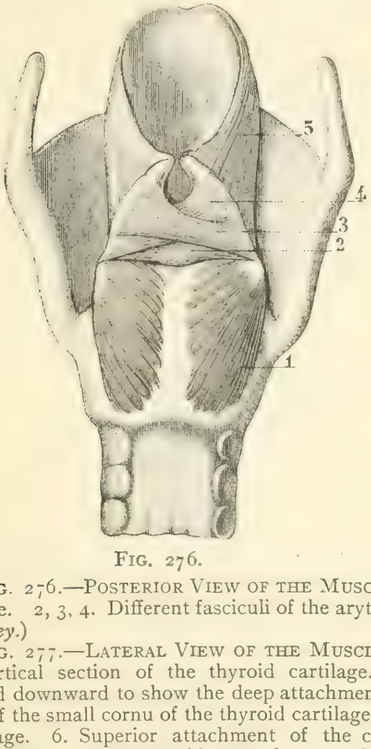

FIG. 276.

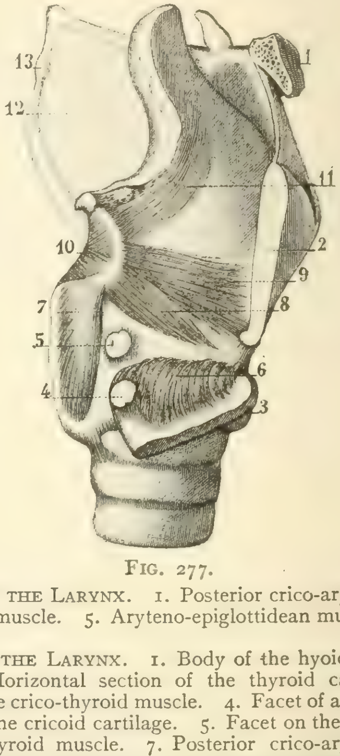

FIG. 277.

FIG. 276.—POSTERIOR VIEW OF THE MUSCLES OF THE LARYNX. 1. Posterior crico-arytenoid muscle. 2, 3, 4. Different fasciculi of the arytenoid muscle. 5. Aryteno-epiglottidean muscle.—(*Sappey.*)

FIG. 277.—LATERAL VIEW OF THE MUSCLES OF THE LARYNX. 1. Body of the hyoid bone. 2. Vertical section of the thyroid cartilage. 3. Horizontal section of the thyroid cartilage turned downward to show the deep attachment of the crico-thyroid muscle. 4. Facet of articulation of the small cornu of the thyroid cartilage with the cricoid cartilage. 5. Facet on the cricoid cartilage. 6. Superior attachment of the crico-thyroid muscle. 7. Posterior crico-arytenoid muscle. 8, 10. Arytenoid muscle. 9. Thyro-arytenoid muscle. 11. Aryteno-epiglottidean muscle. 12. Middle thyro-hyoid ligament. 13. Lateral thyro-hyoid ligament.—(*Sappey.*)

The *lateral crico-arytenoid* muscle arises from the side of the cricoid cartilage. From this point its fibers are directed upward and backward to be inserted into the external process of the arytenoid. Its action is to draw the arytenoid cartilage forward and inward, thus approximating and relaxing the vocal band.

The *thyro-arytenoid* muscle arises from the inferior two-thirds of the inner surface of the thyroid cartilage just external to the median line. From this origin the fibers pass backward and outward, to be inserted into the anterior surface and external angle of the arytenoid cartilage. The inner portion of the muscle lies close to and supports, if it does not constitute a part of, the vocal band. The action of the thyro-arytenoid muscle in conjunction with the lateral crico-arytenoid is to rotate the arytenoid cartilage around the vertical axis and to draw the vocal process forward and inward, thus carrying the vocal cord toward the median line. When the muscles of the two sides simultaneously contract, the vocal bands are closely approximated and the space between them, the *rima vocalis*, reduced to a mere slit, one of the conditions essential to phonation (Fig. 279).

The *arytenoid* muscle consists (1) of transversely arranged fibers which arise from and are inserted into the outer surface of the opposite arytenoid cartilages, and (2) of obliquely directed fibers which arise from the outer angle of one arytenoid to be inserted into the apex of the other. In their course they decussate in the median line. The action of this muscle is to approximate the arytenoid cartilages and thus obliterate that portion of the glottis between the vocal processes, the *rima respiratoria*, and so direct the expiratory blast of air toward and through the rima vocalis.

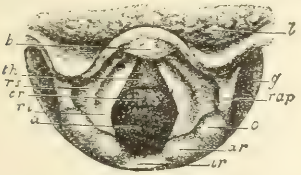

FIG. 278.—GLOTTIS WIDELY OPENED FROM SIMULTANEOUS CONTRACTION OF BOTH CRICO-ARYTENOID MUSCLES. *b.* Epiglottis. *rs.* False vocal band. *ri.* True vocal band. *ar.* Arytenoid cartilages. *a.* Space between the arytenoids. *c.* Cuneiform cartilages. *ir.* Interarytenoid fold. *rap.* Aryepiglottic fold. *cr.* Cartilage rings.—(*Mandl.*)

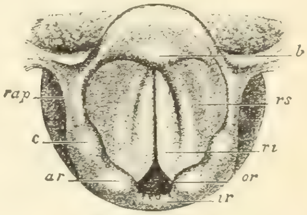

FIG. 279.—POSITION OF THE VOCAL BANDS DUE TO THE SIMULTANEOUS CONTRACTION OF BOTH LATERAL CRICO-ARYTENOID MUSCLES AND BOTH THYRO-ARYTENOID MUSCLES. *b.* Epiglottis. *rs.* False vocal band. *ri.* True vocal band. *or.* Space between the arytenoid cartilages, the *glottis respiratoria.* *ar.* Arytenoid cartilages. *c.* Cuneiform cartilages. *rap.* Aryepiglottic fold. *ir.* Interarytenoid fold.—(*Mandl.*)

The collective actions of the three foregoing muscles is to close or constrict the glottis, and for this reason they are spoken of as the *adductor* or *phonatory* muscles.

The *crico-thyroid* muscle arises from the side and front of the cricoid cartilage and is inserted above into the lower border of the thyroid cartilage. The action of this muscle is to draw up the anterior part of the cricoid cartilage toward the thyroid, which remains stationary, and to swing the quadrate plate of the cricoid and the arytenoid cartilages downward and backward. This movement has the result of tensing the vocal bands. The cricoid is at the same time drawn backward by the action of the more longitudinally disposed fibers.

Nerves of the Larynx.—The nerves which innervate the muscles of the larynx and endow the mucous membrane with sensibility are derived from the vagus trunk. The superior laryngeal is for the most part sensor and distributed to the mucous membrane, though it contains motor fibers for the crico-thyroid muscle. The inferior laryngeal is purely motor and is distributed to all the muscles with the exception of the crico-thyroid.

THE MECHANISM OF PHONATION

Phonation, the production of vocal sounds in the larynx, is the result of the vibration of the vocal bands caused by an expiratory blast of air from the lungs. That a sound may arise it is essential that the glottis be approximately closed and the vocal bands be made more or less tense.

The closure of the glottis—the approximation of the vocal processes and the vocal bands—is accomplished, it will be recalled, by the contraction of the lateral crico-arytenoid, the arytenoid, and the thyro-arytenoid muscles. The increase in tension is accomplished by the contraction of the crico-thyroid and the thyro-arytenoid muscles, the former by the backward displacement of the cricoid and arytenoid cartilages, the latter by converting the natural concave edge of the vocal band to a straight line. The lengthening and tensing of the vocal bands by the crico-thyroid muscle is regarded by some invesigators as a coarse means, the approximation of the free edges by the thyro-arytenoid, as a finer means, of adjustment for the producton of slight changes in the pitch of sounds. The extent to which the glottis is closed and the membranes tensed will depend, however, on the pitch of the sound to be emitted. The appearance presented by the glottis just previous to the emission of a note of medium pitch, as determined by laryngologic examination, is shown in Fig. 280. When the foregoing conditions in the glottis are realized, the air stored or collected in the lungs is forced by the contraction of the expiratory muscles, through the narrow space between the bands. As a result of the resistance offered by this narrow outlet and the force of the expiratory muscles the air within the lungs and trachea is subjected to pressure, and as soon as the pressure attains a certain level the vocal bands are thrown into vibrations, which in turn impart to the column of air in the upper air-passages a corresponding series of vibrations by which the laryngeal vibrations are reinforced. The degree of pressure to which the air in the lungs and trachea is subjected was determined by Latour to vary from 160 mm. of water for sounds of moderate, to 940 mm. of water for sounds of highest intensity. With the escape of the air or the separation of the vocal bands the vibration ceases and the sound dies away.

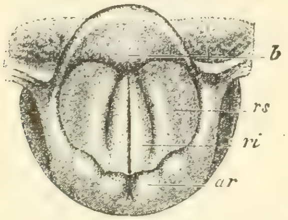

FIG. 280.—POSITION OF THE VOCAL BANDS PREVIOUS TO THE EMISSION OF A SOUND. *b.* Epiglottis. *rs.* False vocal band. *ri.* True vocal band. *ar.* Arytenoid cartilages.—(*Mandl.*)

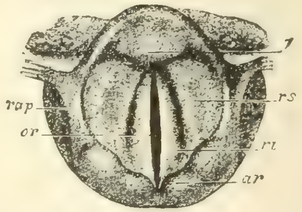

FIG. 281.—POSITION OF THE VOCAL BANDS IN THE PRODUCTION OF NOTES OF LOW PITCH. *l.* Epiglottis. *or.* Glottis. *ns.* False vocal cord. *ni.* True vocal cord. *ar.* Arytenoid cartilages.—(*Mandl.*)

The Characteristics of Vocal Sounds.—In common with the sounds produced by other music instruments, all vocal sounds are characterized by intensity, pitch and quality, tone or color.

The *intensity* or loudness of a sound depends on the extent or amplitude of the to-and-fro vibration or the extent of the excursion of the vocal band on either side of the position of equilibrium or rest; and this in turn depends on the force with which the blast of air strikes the band. The more forceful the blast of air, the larger, other things being equal, will be the primary vibrations of the bands, and hence the secondary vibrations of the air in the upper air-passages.

The *pitch* of the voice depends on the number of vibrations in a unit of time, a second. This will be conditioned by the length of the bands in vibration or the length and width of the aperture through which the air passes and the degree of tension to which the bands are subjected. In the emission of sounds of highest pitch the tension of the vocal bands and the narrowing of the glottis attain their maximum. In the emission of sounds of lowest pitch the reverse conditions obtain. In passing from the lowest to the highest pitched sounds in the range of the voice peculiar to any one individual, there is a progressive increase in both the tension of the vocal bands and the narrowing of the glottic aperture. In the production of low-pitched notes of men, those due to vibrations lying between 80 and 240 per second, the tension is regulated by the crico-thyroid muscle; the aperture of the glottis during this time being elliptic in shape and relatively wide (Fig. 283). In the production of notes due to vibrations lying between 240 and 512 vibrations per second, the anterior fibers of the crico-thyroid muscle relax and the thyro-arytenoid muscle comes into play; by its action the vocal bands are more closely approximated and the vocal aperture reduced to a linear slit. In the high-pitched notes emitted by soprano singers the vocal bands are so closely applied to each other that only a very small portion in front, bounding a small oval aperture, is capable of vibrating (Fig. 282). The difference in the pitch of the voice in men and women is due largely to the greater size and development of the vocal bands in the former than in the latter.

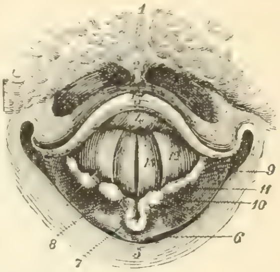

FIG. 282.—GLOTTIS SEEN WITH THE LARYNGOSCOPE DURING THE EMISSION OF HIGH-PITCHED SOUNDS. 1, 2. Base of the tongue. 3, 4. Epiglottis. 5, 6. Pharynx. 7. Arytenoid cartilages. 8. Opening between the true vocal cords. 9. Aryteno-epiglottidean folds. 10. Cartilage of Santorini. 11. Cuneiform cartilage. 12. Superior vocal cords. 13. Inferior vocal cords.—(*Le Bon.*)

The *quality* of the voice, the timbre or tone-color, depends on the *form* combined with the intensity and pitch of the vibration. As with sounds produced by music instruments, the primary or fundamental vibration of the vocal band is complicated by the superposition of secondary or partial vibrations (overtones). The form of the vibration will, therefore, be a resultant of the blending of a number of different vibrations. The quality of the sound produced in the larynx is, however, modified by the resonance of the mouth and nasal cavities; certain of the overtones being reinforced by changes in the shape of the mouth cavity more especially, thus giving to the voice a somewhat different quality.

The Varieties of Voice.—The region of the music scale, comprising all vibrations between 32 and 2048 per second, with which laryngeal sounds are in accord will vary in the two sexes and in different individuals of the same sex. It is customary to classify voices, especially those of singers, into bass, baritone, tenor, contralto, mezzo-soprano, and soprano, in accordance with the regions of the music scale with which they correspond. Thus the succession of notes characteristic of the bass voice vary in pitch from F, fa$_1$, to c′, do$_3$, or from 85 to 256 vibrations per second; those of the baritone from A, la$_1$, to f′, fa$_3$, or from 106 to 341 vibrations per second; those of the tenor from c′, do$_2$, to a′, la$_3$, or from 128 to 427 vibrations per second; those of the contralto from e, mi$_2$, to c″, do$_4$, or from 160 to 512 vibrations per second; those of the mezzo-soprano from g, sol$_2$, to e″, mi$_4$, or from 192 to 640 vibrations per second; those of the soprano from b, si$_2$, to g″, sol$_4$, or from 240 to 768 vibrations per second. The range of the voice is thus seen to embrace from one and three-quarters to two octaves. Some few individual singers have far exceeded this range, but they are exceptional.

Speech is the expression of ideas by means of articulate sounds. These sounds may be divided into vowel and consonant sounds.

The vowel sounds, *a*, *e*, *i*, *o*, *u*, are laryngeal tones modified by the superposition and reinforcement of certain overtones developed in the mouth and pharynx by changes in their shapes. The number of vibrations underlying the production of each vowel sound is a matter of dispute.

Consonant sounds are produced by the more or less complete interruption of the vowel sounds during their passage through the organs of speech. These may be divided into:

1. Labials, *p*, *b*, *m*.
2. Labio-dentals, *f*, *v*.
3. Linguo-dentals, *s*, *z*.
4. Anterior linguo-palatals, *t*, *d*, *l*, *n*, *r*, *sh*, *zh*.
5. Posterior linguo-palatals, *k*, *g*, *h*, *y*.

The names of these different groups of consonants indicate the region of the mouth in which they are produced and the means by which the air blast is interrupted.

THE NERVE MECHANISM OF THE LARYNX

The nerve mechanism by which the musculature of the larynx is excited to action and coördinated so as to subserve both respiration and phonation involves the fibers contained in the superior and inferior laryngeal nerves (both branches of the vagus) and their related nerve-centers in the central nerve system.

For respiratory purposes it is essential that the lumen of the glottis shall be sufficiently large to permit the entrance and exit of air without hindrance. Laryngoscopic examination of the larynx in the human being shows that during *quiet* respiration the vocal bands are widely separated and almost stationary, moving but slightly during either inspiration or expiration. At this time, according to the investigations of Semon, the area of the glottis is approximately 160 sq. mm., somewhat less than the area of either the supraglottic or infraglottic regions, which is about 200 sq. mm. This condition of the glottis is maintained by the steady continuous contraction of the posterior crico-arytenoid muscles, the *abductors of the vocal bands*.

For phonatory purposes it is essential that the respiratory function be temporarily suspended and the vocal bands closely approximated. This is accomplished by the contraction of the remaining muscles of the larynx, with the exception of the crico-thyroid, which are collectively known as the *adductors of the vocal bands.* During phonation the adductor muscles overcome the activity of the abductors. With the cessation of phonation the abductors immediately restore the vocal bands to their former respiratory position.

The activities of these two antagonistic groups of muscles are under the control of the central nerve system. The only pathway for the excitator nerve impulses is through the fibers of the inferior or recurrent laryngeal nerve. The relation of these nerve-fibers both centrally and peripherally, as well as their physiologic action, has been the subject of much experimentation. The results have not always been in accord, owing to the choice of animal, the use of anesthetics, strength of stimulus, etc.

As the outcome of many investigations it is believed that each muscle group is innervated by its own bundle of nerve-fibers, both of which are contained in the inferior laryngeal, though coming from two separate centers in the medulla oblongata. Russell succeeded in separating the fibers for the abductors from the fibers for the adductors in the inferior laryngeal, and in tracing them to their terminations. So completely was this done that it became possible to produce at will, through stimulation, either abduction or adduction, without contraction of the muscle of opposite function.

The *laryngeal respiratory center* was located by Semon and Horsley, in the cat, in the upper part of the floor of the fourth ventricle. Stimulation of this area during etherization was followed by abduction of the vocal bands. The efferent fibers of this center are believed by some investigators to leave the central nerve system in the spinal accessory nerve, by others in the lower roots of the vagus.

From the continuous activity of the abductor muscle, and the stationary position of the vocal bands, it is probable that the medullary center is in a state of continuous activity or tonus, the result probably of reflex influences.

A cortical representation for laryngeal respiratory movements has been determined by Semon and Horsley in different classes of animals. In the cat especially, stimulation of the border of the olfactory sulcus gives rise to complete abduction of the vocal bands on both sides. The representation is therefore bilateral.

The *phonatory center* was located by the same investigators in the medulla near the ala cinerea and the upper border of the calamus scriptorius. Stimulation of this area was invariably followed by bilateral adduction of the vocal bands and closure of the glottis.

A cortical representation for phonatory movements has also been located in the lower portion of the pre-central convolution, near the anterior border. Stimulation of this area gives rise to marked adduction of both vocal bands, indicating that the representation is therefore bilateral.

Faradic stimulation of the inferior laryngeal nerve during slight ether anesthetization gives rise to closure of the glottis; the same stimulation, however, during deeper anesthetization gives rise to opening or dilatation of the glottis, a fact indicating that either the adductor muscles or their nerve terminals are depressed by the action of the ether before the muscles and nerves of opposite function. The superior laryngeal nerves contain motor fibers for the crico-thyroid muscles. Stimulation of the nerve gives rise to contraction of the muscle and increased tension of the vocal bands. It is believed that these fibers are derived originally from the efferent fibers of the glosso-pharyngeal nerve. The remaining fibers of the superior laryngeal endow the upper portion of the larynx with extreme sensibility which to a certain extent protects the air-passages against the entrance of foreign bodies. Irritation of the terminal filaments of this nerve by particles of food, solid or liquid, gives rise to marked reflex spasm of the adductor muscles and closure of the glottis, followed by a strong expiratory blast of air from the lungs by which the offending particles are removed. *Division* of this nerve on both sides is followed by a paralysis of the crico-thyroid muscles, a lowering of the tension of the vocal bands, and a loss of sensibility of the laryngeal mucous membrane.

CHAPTER XXVIII

THE SENSES OF TOUCH, TASTE AND SMELL

Introductory.—It is one of the functions of the nerve system to bring the individual into conscious relation with the external world. This is accomplished in part through the intermediation of afferent nerves, connected peripherally with highly specialized terminal organs, and centrally with specialized areas in the cerebral cortex.

Excitation of the terminal organs by material changes in the environment develops nerve impulses which, transmitted to the cortical areas, evoke sensations. These sensations, differing in character from those vague ill-defined sensations—*e.g.*, fatigue, well-being, discomfort, etc.—caused by material changes occurring within the body, are termed special sensations—*e.g.*, touch; pressure; pain; temperature; taste; smell; light and its varying qualities, intensity, hue, and tint; sound and its varying qualities, intensity, pitch, and timbre.

The terminal organs which receive the impress of the external world are the skin, tongue, nose, eye, and ear, and collectively constitute the special sense-organs. The physiologic mechanisms which underlie and develop these special sensations are known respectively as the tactile, gustatory, olfactory, optic, and auditory. Each mechanism responds to but a single form of stimulus and to no other. Thus, the stimulus for the skin is mechanic pressure; for the tongue, soluble organic and inorganic matter; for the nose, volatile or gaseous matter; for the eye, ether vibrations; for the ear, atmospheric undulations. These stimuli alone are adequate to the physiologic excitation of the different mechanisms.

The factors involved in the production of the sensations include (1) a special physical stimulus; (2) a specialized terminal organ; (3) an afferent nerve pathway, and (4) a specialized receptive sensor cell in the cerebral cortex.

Though the resulting sensations in each instance differ widely in their characteristics, it is difficult to present a satisfactory explanation for these differences. If it be assumed that the nerve impulses which ascend the different nerves of special sense are alike in quality, then it must be admitted that the character of the sensation is the expression of a specialization and organization of the cortical area. If, on the other hand, specialization of the cortex is denied, then there must be admitted a specialization of the peripheral organ—with a resulting difference in quality or rapidity of the nerve impulses which would impress or excite the non-specialized cortex in such a way as to call forth the characteristic sensation. It is possible, however, that neither supposition is wholly correct, and that the character of the sensation depends on the construction and adaptation of the entire sense apparatus to the character of the stimulus.

Whatever the conditions for their origin and whatever their characteristics, sensations in themselves do not constitute knowledge; they are but elementary states of consciousness, raw materials out of which the mind elaborates conceptions and forms judgments as to the character of any given object in comparison with former experiences.

THE SENSE OF TOUCH

The physiologic mechanism involved in the sense of touch includes the skin and the mucous membrane lining the mouth, the afferent nerves, their cortical connections, and nerve-cells in the cortex of the parietal lobe.

Peripheral excitation of this mechanism develops nerve impulses which, transmitted to the cortex, evoke sensations of touch and temperature. To the skin, therefore, is ascribed a touch sense and a temperature sense. Of the touch sensations two kinds may be distinguished: viz., pressure sensations and place sensations. With the contact of an external body there arises the perception not only of the pressure, but also the perception of the place or locality of the contact. In accordance with this, it is customary to attribute to the skin a pressure sense and a location sense.

The specific physiologic stimuli to the terminal organs in the skin and oral mucous membrane are mechanic pressure and thermic vibrations.

The Skin.—The skin, which constitutes the basis for the sense of touch, covers and closely invests the entire body. It varies in thickness and delicacy in different regions, though its structure is everywhere essentially the same. As the physiologic anatomy of the skin has elsewhere been detailed (page 472), it is only necessary to state here that it is divided into a deep and a superficial layer. The *former*, known as the *derma*, consists of an inner layer of rather loose connective tissue and an outer layer of condensed connective tissue. The *latter*, known as the *epidermis*, consists of an inner layer of pigment cells and a thick outer layer of epithelial cells. The derma is characterized by the presence of elevations (papillæ) which are everywhere extremely abundant. Throughout the derma ramify blood-vessels and nerves.

The Peripheral or Terminal Organs.—Between the contact surface and the afferent nerves specialized structures are found which serve as intermediatos between the stimulus, on the one hand, and the afferent nerves, on the other hand. By virtue of their structure they are far more irritable than the nerve-fibers and hence respond more quickly to the physiologic stimulus than the nerve-fiber itself. To these specialized organs, found not only in the skin but in other sense-organs as well, the term peripheral or terminal organ is given. It is these structures that are primarily excited to activity by the physiologic stimulus, and that in turn arouse the nerve to activity. Peripheral organs are to be regarded as special modes of termination of afferent nerves adapted for the impress of a specific stimulus. The peripheral organs of afferent nerves found in the skin and oral mucous membrane present a variety of forms, some of which are as follows:

1. *Free Endings.*—These are pointed or club-shaped processes, the ultimate terminations of afferent nerve-fibrils, found in and among epidermic cells.
2. *Tactile Cells.*—These are oval nucleated bodies found in the deeper layers of the epidermis. They rest upon or are embraced by a crescentic-shaped body, the *tactile meniscus*, which in turn is directly connected with the nerve-fibril and probably a modification of it.
3. *The Corpuscles of Meissner and Wagner.*—In the papillæ of the derma, especially in the palm of the hand and in the finger-tips, are found elliptical bodies consisting of a connective-tissue capsule containing a number of tactile discs with which the nerve-fibrils are connected. If

the afferent nerve is traced to the capsule, it is found to lose both its neurilemma and its medulla, after which the naked fibril penetrates the capsule, breaks up into a number of branches, and after pursuing a more or less spiral course becomes connected with the tactile discs.

4. *Hair Wreaths.*—Just below the openings of the sebaceous glands the hair-follicles are surrounded by naked axis-cylinder fibrils in the form of a wreath, which in all probability terminate in the cells of the external root-sheath. These, too, are to be regarded as part of the touch apparatus.
5. *Corpuscles of Vater or Pacini.*—These are oval-shaped structures found along the nerves distributed to the palms of the hands and the soles of the feet, on the nerves distributed to the external genital organs, to joints and other structures. They consist of a thick capsule of lamellated connective tissue in the interior of which is a bulb resembling granular protoplasm. The axis-cylinder of the nerve-fiber enters the capsule and becomes connected with the bulb.

Other forms of peripheral organs are found in special regions of the skin as well as in different animals.

Touch Sense.—The area, stimulation of which evokes sensations of touch is coextensive with the skin and that limited portion of the mucous membrane lining the mouth. Careful stimulation of the skin by means of a fine stiff bristle has revealed the fact, however, that the touch area is not continuous, but discrete, presenting itself under the form of small areas or spots, separated by relatively large areas insensitive to the same agent. Stimulation of these spots always calls forth a sensation of touch. For this reason they are known as "touch spots." The number of such spots in any given area of skin varies considerably. Thus, in the skin of the calf fifteen such spots have been counted in a square centimeter. In the palm of the hand from forty to fifty have been counted in an area of the same extent. They are also especially abundant in the immediate neighborhood of the hair-follicles.

The peripheral end-organ associated with the touch spots in the neighborhood of a hair-follicle is in all probability the wreath of nerve-fibrils surrounding the follicle. In regions devoid of hairs the end-organ is the Meissner corpuscle, for in the palmar surface of the distal phalanx of the index-finger, where the touch sense is quite acute, about 20 corpuscles are present in each square millimeter of surface. The specific stimulus necessary to evoke the sensation of touch is a deformation of the skin; and the greater this is, within physiologic limits, the more pronounced is the sensation.

Pressure Sense.—The contact of an external body is attended by a certain amount of pressure, which, however, must attain a certain degree before the sensation can be evoked. This is known as the threshold value, or the degree of liminal intensity. Since the sensations are the result of pressure, they are termed pressure sensations, and their intensity may be expressed in terms of pressure.

The sensitivity of the skin as determined by the pressure sense varies in different regions of the body and in accordance with the size of the area pressed. Thus, the liminal intensity of a stimulus for an area of nine square millimeters for the skin of the forehead is 0.002 gram; for the flexor aspect of the forearm, 0.003 gram; and for the hips, thigh, and abdomen, 0.005 gram; for the palmar surface of the finger, 0.019 gram; for the heel, 1 gram.

The delicacy of the sense of touch is measured by the slight increase or decrease in the intensity of the stimulus that will produce an appreciable change in the intensity of the sensation. Not all changes in the stimulus, however, are attended by a change in the sensation. It has been determined that the latter will change only when the former changes in a definite ratio, which for the volar surface of the third phalanx of the index-finger is as 29 is to 30. Thus, other things being equal, a sensation caused by a given weight will only change with moderate stimulation when one-thirtieth of the weight is either added or subtracted. The ratio of change, however, varies in different regions of the body: thus, for the back of the hand the ratio varies from one-tenth to one-twentieth; for the tongue, one-thirtieth to one-fortieth. The difference of stimulus necessary to evoke a sensation is known as the threshold difference. It seems to be a law not only for the skin, but for other senses as well, that a change in the intensity of a sensation, to an appreciable extent, will occur only when the objective stimulus changes in a definite ratio. This ratio, however, will vary not only in different regions of the skin, in different individuals, but with the sense-organ investigated.

Place Sense.—The sensation evoked by stimulation of the skin is always, under normal conditions, referred to the place stimulated. This holds true not only for two or more points near or widely separated on the same side, but also for corresponding points on opposite sides of the body, even when the stimuli have the same intensity and are simultaneously applied. The cause for this localizing power is to be found in a difference in the quality of the sensation related in some way to the part stimulated. Each cutaneous area is supposed to give to the tactile sensation a quality or *local sign* by virtue of which the mind is enabled to localize the point of contact.

Each cutaneous area which has a local sign of its own is known as a sensor circle, for the reason that the mind does not refer the sensation to a point, but to an area more or less circular in outline. The skin may, therefore, be regarded as composed of myriads of such circles varying in size in different regions of the body.

The delicacy of the localizing power in any part of the skin is determined by testing the power which the part possesses of distinguishing the sensations produced by the contact of the points of a pair of compasses placed close together. The distance to which the points must be separated in order to evoke two separate recognizable sensations is a measure of the diameter of the sensor circle. Within this circle the two sensations become fused into one sensation. The discriminative sensibility of different regions as determined by compass points is shown in the following table; the numbers represent the distances at which two sensations are recognized:

	mm.
Tip of tongue	1.1
Palmar surface of third phalanx of index-finger	2.2
Red surface of lips	4.5
Palmar surface of first phalanx of finger	5.5
Tip of nose	6.8
Palm of hand	8.9
Lower part of forehead	22.6
Dorsum of hand	31.6
Dorsum of foot	40.6
Middle of the back	67.7

The discriminative sensibility of any portion of the body is a function of its mobility. This is shown by the fact that it increases rapidly from the shoulders to the fingers and from the hips to the toes.

The Temperature Sense.—The sensations of heat and cold which are experienced from time to time are caused by changes in the temperature of the skin produced in a variety of ways. As these sensations are specifically different from those of touch, as well as different from each other, it is highly probable that for each sensation there are special nerve-endings distributed throughout the skin. Investigations have shown that all over the skin there are innumerable spots of varying size which if stimulated evoke sensations of heat or cold. Such points are termed heat and cold spots. Each responds to but one kind of stimulus. A warm object applied to a heat spot will evoke a sensation of warmth. It will have no effect on the cold spot. The reverse is also true. Between the cold and heat spots there are areas that are neutral, insensitive to either heat or cold. The cold spots are more numerous than the heat spots in almost all regions of the body. (See Fig. 283.)

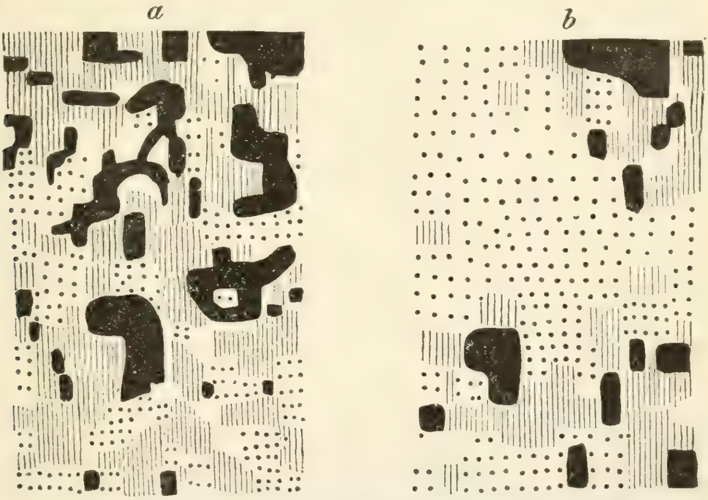

FIG. 283.—COLD AND HOT SPOTS FROM THE ANTERIOR SURFACE OF THE FOREARM. *a.* Cold spots. *b.* Hot spots. The dark parts are the most sensitive, the hatched the medium, the dotted the feebly, and the vacant spaces the non-sensitive.—(*Landois and Stirling.*)

The sensitivity of the skin to temperature changes is very acute, as shown by the fact that even 0.05°C. is readily appreciable. This holds true, however, only when the temperature of the object lies between 27° and 33°C. This capability varies in different regions of the skin, and depends on the number of heat and cold spots present, the thickness of the epidermis, the thermal conductivity of the object touching it, and the extent to which it is habitually exposed or protected.

The physiologic stimulus to the thermic end-organs is the passage of heat through the skin from the interior of the body to the surrounding air. If the radiation is continuous and uniform, the end-organs soon adapt themselves to the temperature of the surrounding air and the sensation of heat, under physiologic conditions, is not evoked. If there is a sudden rise in the external temperature caused by natural or artificial means, which diminishes the radiation, the temperature of the skin will at once rise, the end-organs will be stimulated, and a sensation of warmth developed. If, on the other hand, there is a sudden fall in temperature and an increased radiation, the temperature of the skin will fall, the end-organs will be stimulated, and a sensation of cold developed. Experiment also teaches that the intensity of a warm or cold sensation will depend on the existing temperature of the skin, and not upon the absolute temperature of the object. Thus, water at 20°C. will evoke a sensation of heat or cold respectively according as the skin has previously been cooled below or warmed above this temperature.

The Muscle Sense.—As a result of the activities of the musculature of the body or even of its individual parts, there arises in consciousness a series of sensations which are termed muscle sensations. These sensations give rise to the perception—

1. Of the direction and duration of both passive (due to external causes) and active movements (due to internal, volitional efforts) which take place without hindrance;
2. Of the resistance offered to movements by external bodies; and
3. Of the posture of the body or of its individual parts.

As to the seat of the physiologic processes which precede and underlie the development of the sensations two views, at least, may be advanced, viz.:

1. That the processes are central in origin and partake of the nature of a discharge of nerve impulses from the nerve-cells through the motor nerves to the muscles, the entire process being accompanied by sensation. This is known as the innervation theory.
2. That the processes are peripheral in origin, initiated by stimulation of specialized end-organs in the muscles and tendons which are connected through the intermediation of afferent nerves with nerve-cells in the cerebral cortex.

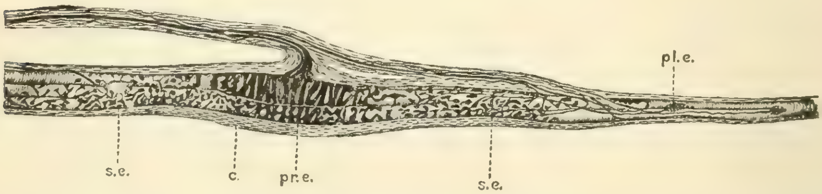

FIG. 284.—A NEURO-MUSCLE SPINDLE OF A CAT. (*Ruffini.*) *c.* Capsule. *pr. e.* Primary ending. *s. e.* Secondary ending. *pl. e.* Plate ending. (All these are probably sensor in function.) —(*Starling's "Physiology."*)

The physiologic mechanism subserving the muscle sense, according to the second theory, now held by many physiologists, thus involves peripheral end-organs, afferent nerves, their cortical connections and nerve-cells in the cerebral cortex at or near the junction of the superior and inferior parietal convolutions.

The End-organs.—These are small fusiform structures found in and among the muscle bundles of all the muscles of the body with the exception of the diaphragm and eye muscles. In the muscles of the arm and in the small muscles of the hand they are especially abundant. From their shape they are known as *muscle spindles.* They vary in length from 2 to 12 mm.

and in breadth from 0.15 to 0.4 mm. Each spindle (Fig. 284) consists of a connective-tissue capsule containing from two to ten longitudinally arranged striated muscle-fibers of fine diameter. In the middle or equatorial region of these *intra-fusal* fibers there is frequently found a quantity of non-striated protoplasmic matter. The spindle is supplied with both sensor and motor nerves. The sensor fiber loses its external investments as it approaches the capsule. The naked axis-cylinder then penetrates the capsule, and after dividing several times terminates in a ribbon-like or spiral manner around the intra-fusal muscle-fiber. This ending was described by and is known as Ruffini's "annulo-spiral ribbon." The motor nerve also penetrates the capsule and terminates in the polar extremities of the intra-fusal fiber. Sensor end-organs supposed to be connected with the muscle sense are also found in the tendons of muscles.

Afferent Nerves.—That muscles are abundantly supplied with afferent nerves has been proved by different methods of investigation. With histologic methods Sherrington has traced afferent fibers from the muscle spindles directly into the spinal nerve ganglia. The contractions of muscles from electric stimulation as well as the contractions known as muscle cramp, due to unknown agents, give rise to sensations of pain, a fact which indicates the presence in muscles of afferent or sensor nerves.

Cortical Area.—Pathologic findings have shown that an impairment or a loss of the muscle sense is associated with destructive lesions of perhaps the super- and sub-parietal convolutions (Figs. 249 and 252). In a case reported by Starr the removal of a small tumor in the pia mater situated over the junction of the superior and inferior parietal lobules was followed by a loss of the muscle sense and marked ataxia in the right hand for a period of six weeks, after which recovery took place. These symptoms were attributed to injury of the cortex from unavoidable surgical procedures.

The muscle sensations, as stated in foregoing paragraphs, form the basis of the perception not only of the direction and the duration of a body movement and the resistance experienced, but also of the position and the tension of the muscle groups. The latter fact more especially makes it possible for the mind to direct the muscles and to graduate the energy necessary to the accomplishment of a definite purpose.

Active Touch.—Active touch or the application of the fingers to the surfaces of external objects implies the coöperation of the skin and the muscles. The sensations which are evoked are combinations of contact and muscle sensations. The union of these sensations forms the basis of the perception of hardness, softness, smoothness, and roughness of bodies.

THE SENSE OF TASTE

The physiologic mechanism involved in the sense of taste includes the tongue, the gustatory nerves, their cortical connections and nerve-cells in the gray matter of the sub-collateral convolution. The peripheral excitation of this apparatus gives rise to nerve impulses which transmitted to the brain evoke the sensations of taste. The specific physiologic stimulus is matter, organic and inorganic, in a state of solution.

The nerves of taste contained in the trunks of the chorda tympani (page 630) and of the glosso-pharyngeal (page 634) after entering the medulla oblongata terminate around certain sensor end nuclei, the exact location of which is uncertain. From these nuclei axons arise which in all probability cross the median plane and ascend to the sub-collateral convolution. The exact course of this gustatory tract is, however, obscure.

The Tongue.—The tongue consists of both intrinsic and extrinsic muscles, in virtue of which it is susceptible of a change both in shape and in position. The movements of the tongue, though not essential to taste, are made use of in the finer discrimination of tastes.

The tongue is covered over by mucous membrane continuous with that lining the oral cavity. The dorsum of the tongue presents a series of papillæ richly supplied with blood-vessels and nerves. Of these there are three varieties, the filiform, the fungiform, and the circumvallate.

1. The *filiform papillæ*, the most numerous, cover the anterior two-thirds of the tongue; they are conical or filiform in shape and covered with horny epithelium which is often prolonged into filamentous tufts.
2. The *fungiform papillæ*, found chiefly at the tip and sides of the tongue, are less numerous but larger than the preceding and of a deep red color.
3. The *circumvallate papillæ*, from eight to ten in number, are situated at the base of the tongue arranged in the form of the letter V. They consist of a central projection surrounded by a wall or circumvallation from which they take their name.

The Peripheral End-organs. The Tastebuds.—Embedded in the epithelium covering the mucous membrane not only of the tongue but of the palate and posterior surface of the epiglottis are small ovoid bodies which from their relation to the gustatory nerves are regarded as their peripheral end-organs and known as taste-buds or taste-beakers. Each bud is ovoid in shape (Fig. 285). Its base rests on the tunica propria; its apex comes up to the epithelium, where it presents a narrow funnel-shaped opening, the *taste-pore*. The wall of the bud is composed of elongated curved epithelium. The interior contains narrow spindle-shaped neuro-epithelial cells provided at their outer extremity with stiff hair-like filaments which project into the taste-pore.

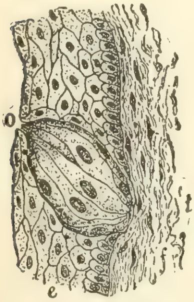

FIG. 285.—TASTE-BUD FROM CIRCUMVALLATE PAPILLA OF A CHILD. The oval structure is limited to the epithelium (*e*) lining the furrow, encroaching slightly upon the adjacent connective tissue (*f*); *o*, taste-pore through which the taste-cells communicate with the mucous surface. —(*After Piersol.*)

The neuro-epithelial cells are in physiologic relation with the nerves of taste. The terminal branches, after entering the bud at its base, develop fine tufts which come into contact with the cells. That the taste-buds are connected with the nerves of taste is rendered probable from the fact of their degeneration after division of the nerves.

The Taste Area.—The taste area, though confined for the most part to the tongue, extends in different individuals to the mucous membrane of the hard palate, to the anterior surface of the soft palate, to the uvula, the anterior and posterior half arches, the tonsils, the posterior wall of the pharynx, and the epiglottis.

The Taste Sensations.—The sensations which arise in consequence of impressions made by different substances on the peripheral apparatus of this area are in so many instances combinations of taste, touch, temperature, and smell that they are extremely difficult of classification. Nevertheless six primary tastes can be recognized: bitter, sweet, acid or sour, salt or saline, alkaline and metallic. Though the contact of any bitter, sweet, acid, salt, etc., substance with any part of the tongue will, if the substance be present in sufficient quantity or concentration, develop a corresponding sensation, some regions of the tongue are more sensitive and responsive than others. Thus, the posterior portion is more sensitive to bitter substances than the anterior; the reverse is true for sweet substances and perhaps for acids and salines.

The intensity of the resulting sensation in any given instance will depend on the degree of concentration of the substance, while its massiveness will depend on the area affected.

THE SENSE OF SMELL

The physiologic mechanism involved in the sense of smell includes the nasal fossæ, the olfactory nerves, the olfactory tracts, and nerve-cells in those areas of the cortex known as the uncinate convolution and anterior part of the gyrus fornicatus. Peripheral stimulation of this mechanism develops nerve impulses which, transmitted to the cortex, evoke the sensations of odor. The specific physiologic stimulus is matter in the gaseous or vaporous state.

The Nasal Fossæ.—The nasal fossæ are irregularly shaped cavities separated by a vertical septum formed by the perpendicular plate of the ethmoid bone, the vomer, and the triangular cartilage. The outer wall presents three recesses separated by the projection inward of the turbinated bones. Each fossa opens anteriorly and posteriorly by the anterior and posterior nares, the latter communicating with the pharynx. Both fossæ are lined throughout by mucous membrane. The upper part of the fossa is known as the olfactory, the lower portion as the respiratory region. In the former, the mucous membrane over the septum and superior turbinated bone is somewhat thicker than elsewhere and covered with a neuro-epithelium which constitutes

The Peripheral End-organ.—This consists of a basement membrane supporting two kinds of cells, the olfactory and the sustentacular. The olfactory cells are bipolar nerve-cells, the center of which contains a large spheric nucleus. The peripheral pole is cylindric or conic in shape and provided at its extremity with several hair-like processes. The central pole becomes the axon process and passes directly to the olfactory bulb.

The sustentacular cells are epithelial in character and, as their name implies, support or sustain the olfactory cells.

For the appreciation of odorous particles the air must be drawn through the nasal fossæ with a certain degree of velocity. If the particles are widely diffused in the air, they must be drawn not only more quickly but more forcibly into contact with the olfactory hairs, as in the act of sniffing, the result of short energetic inspirations. To many substances the olfactory apparatus is extremely sensitive. Thus, it has been shown that a particle of mercaptan the actual weight of which was calculated to be $\frac{1}{460,000,000}$ of a milligram gives rise to a distinct sensation.

The Olfactory Sensations.—The sensations which arise in consequence of the excitation of the olfactory apparatus are very numerous and their classification is extremely difficult. For this reason it is customary to divide them into two groups: viz., agreeable and disagreeable, in accordance with the feelings they excite in the individual. As the olfactory sensations give rise to feelings rather than ideas, this sense plays in man a subordinate part in the acquisition of knowledge. In lower animals this sense is employed for the purpose of discovering and securing food, for detecting enemies and friends, and for sexual purposes. In land animals the entire olfactory apparatus is well developed and the sense keen; in some aquatic animals, as the dolphin, whale, and seal, the apparatus is poorly developed and the sense dull.

CHAPTER XXIX

THE SENSE OF SIGHT

The physiologic mechanism involved in the sense of sight includes the eyeball, the optic nerve, the optic tracts, the thalamo-occipital tract or the optic radiation, and nerve-cells in the cuneus and adjacent gray matter. Peripheral stimulation of this mechanism develops nerve impulses which transmitted to the cortex evoke (1) the sensation of light and its different qualities—colors; (2) the perception of light and color under the form of pictures of external objects; and (3) in connection with the ocular muscles, the production of muscle sensations by which the size, distance, and direction of objects may be judged.

The specific physiologic stimulus to the terminal end-organ, the retina, is the impact of ether vibrations. In general, it may be said that, at least for the same color, the intensity of the objective vibration determines the intensity of the sensation.

THE PHYSIOLOGIC ANATOMY OF THE EYEBALL

The eyeball is situated at the fore part of the orbit cavity, and in such a position as to permit of an extensive range of vision. It is loosely held in position by a fibrous membrane, the capsule of Tenon, which is attached, on the one hand, to the eyeball itself, and, on the other, to the walls of the orbit cavity. Thus suspended, the eyeball is susceptible of being turned in any direction by the contraction of the muscles attached to it.

The ball is spheroid in shape, measuring about 24 millimeters in its antero-posterior diameter and a little less in its transverse and vertical diameters. When viewed in profile, it is seen to consist of the segments of two spheres, of which the posterior is the larger, occupying five-sixths, and the anterior is the smaller, occupying one-sixth of the ball.

If a horizontal section of the eyeball is made it will be seen to consist of several concentrically arranged membranes enclosing various refracting media essential to vision. (See Fig. 286.)

The membranes, enumerating them from without inward, are as follows: the sclera and cornea, the chorioid and iris, and the retina. The refracting media are the aqueous humor, the crystalline lens, and the vitreous humor.

The Sclera and Cornea.—The *sclera* is the thick opaque membrane covering the posterior five-sixths of the ball. It is composed of layers of connective tissue which are arranged transversely and longitudinally. It is pierced posteriorly by the optic nerve about 3 or 4 millimeters internal to the optic axis. By virtue of its firmness and density the sclera gives form to the eyeball, protects delicate structures enclosed by it, and serves for the attachment of the muscles by which the ball is moved. The *cornea* is the transparent membrane forming the anterior one-sixth of the ball It is nearly circular in shape, measuring in its horizontal meridian 12 mm., in its vertical meridian 11 mm. The curvature is, therefore, sharper in the latter than in the former. The radius of curvature of the anterior surface at that central portion ordinarily used in vision is 7.829 mm.; that of the posterior surface about 6 mm.

The substance of the cornea is made up of thin layers of delicate transparent fibrils of connective tissue continuous with those found in the sclera. Lymph-spaces are present throughout the cornea, in which are to be found lymph-corpuscles. The anterior surface of the cornea is covered with several layers of nucleated epithelium supported by a structureless membrane, the *anterior elastic lamina*. The posterior surface also is covered by a layer of epithelium supported by a similar membrane, the *posterior elastic lamina* or the membrane of Descemet, which at its periphery becomes continuous with the iris. At the junction of the cornea and sclera there is a circular groove, known as the canal of Schlemm.

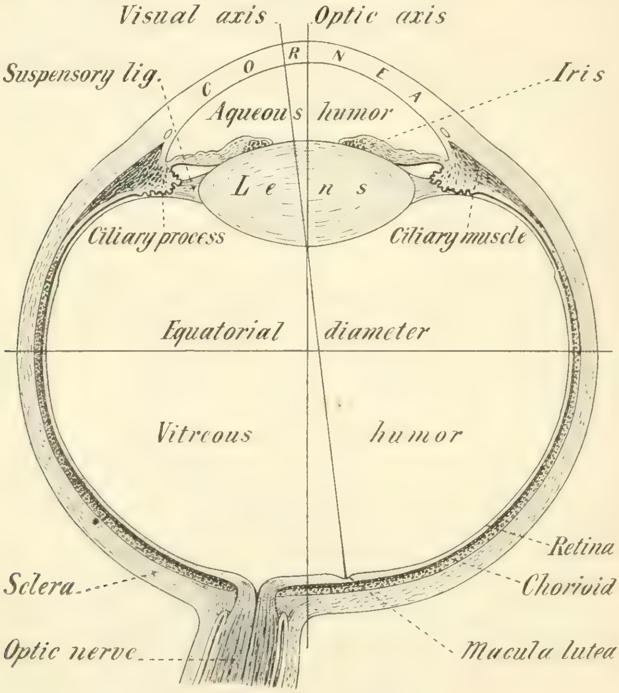
Visual axis
Optic axis
Suspensory lig.
Iris
C O R N E A
Aqueous humor
L e n s
Ciliary process
Ciliary muscle
Equatorial diameter
Vitreous humor
Retina
Chorioid
Sclera
Optic nerve
Macula lutea

Fig. 286.—The Right Eye viewed in Horizontal in Section.—(*After Toldt.*)

The posterior elastic lamina, near the margin of the cornea, breaks up into fibers to form a network structure, the intervals between the fibers of which are known as the spaces of Fontana. These spaces are in communication with the canal of Schlemm.

The Chorioid, Iris, Ciliary Muscle, and Ciliary Processes. *The Chorioid.*—The chorioid is the dark brown membrane which extends forward nearly to the cornea, where it terminates in a series of folds, the ciliary processes. Posteriorly, it is pierced by the optic nerve. It is composed largely of blood-vessels, arteries, capillaries, and veins, supported by connective tissue. Externally it is loosely connected to the sclera; internally it is lined by a layer of hexagonal cells containing black pigment which though usually described as a part of the chorioid, are now known to belong, embryologically and physiologically, to the retina. Lying within the outer layer of arteries and veins there is a thick layer of small arterioles and capillaries, known as the chorio-capillaris. The chorioid with its contained blood-vessels bears an important relation to the nutrition and function of the eye. It provides a free supply of lymph and presents a uniform temperature to the retina in contact with it.

The Iris.—The iris is the circular, variously colored membrane in the anterior part of the eye just behind the cornea. It presents a little to the nasal side of the center a circular opening, the *pupil.* The outer or circumferential border is united by connective tissue to the cornea, sclera, and ciliary muscle; the inner border forms the boundary of the pupil. The iris consists of a framework of connective tissue supporting blood-vessels, muscle-fibers, and pigmented connective-tissue cells. The anterior surface is covered by a layer of cells continuous with those covering the posterior surface of the cornea. The posterior surface is formed by a thin structureless membrane supporting a layer of pigment cells continuous with those lining the chorioid. The color which the iris presents in different individuals depends on the relative amount of pigment in the connective-tissue corpuscles. In blue eyes the pigment is wanting. In gray, brown, and black eyes the pigment is present in progressively increasing amounts. The blood-vessels are connected with those of the chorioid coat.

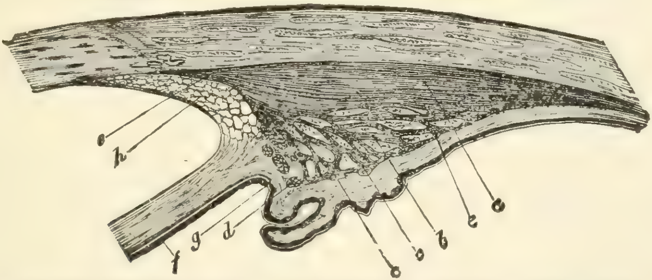

FIG. 287.—SECTION THROUGH THE CILIARY REGION OF THE HUMAN EYE. *a.* Radiating bundles of the ciliary muscle. *b.* Deeper bundles. *c.* Circular network. *d.* Annular muscle of Müller. *e.* Tendon of ciliary muscle. *f.* Muscle-fibers on posterior side of the iris. *g.* Muscles on the ciliary border of the same. *h.* Ligamentum pectinatum.—(*After Iwanoff.*)

The muscle-fibers are of the non-striated variety and arranged in two sets, one circularly, the other radially, disposed.

The circular fibers are found close to the pupil near the posterior surface of the iris. Contraction of this band of fibers diminishes, relaxation increases, the size of the pupil. This muscle is known as the *sphincter pupillæ* or *sphincter iridis.*

The radial fibers form a more or less continuous layer in the posterior part of the iris, extending from the margin of the pupil, where they blend with the circular fibers, to the outer border. Contraction of the fibers increases the size of the pupil. The muscle is known as the *dilatator pupillæ.*

The nerves exciting the *sphincter pupillæ* to action are the ciliary nerves, axons of nerve-cells located in the ciliary or ophthalmic ganglion. Stimulation of these fibers gives rise to contraction of the sphincter and diminution in the size of the pupil. The nerves exciting the *dilatator pupillæ* to action are axons of nerve-cells located in the superior cervical ganglion. They reach the iris by way of the cervical sympathetic, the ophthalmic division of the fifth, and the long ciliary nerve. Stimulation of these nerves is followed by contraction of the dilatator and an increase in the size of the pupil. Both the ciliary and superior cervical ganglia are in relation with pre-ganglionic fibers coming from the central nerve system (see page 653).

The Ciliary Muscle.—The ciliary muscle is a gray circular band about two millimeters in width, consisting of non-striated muscle-fibers. The majority of these fibers pursue a radial or meridional direction. Taking their origin from the junction of the sclera, cornea, and iris, they pass backward to be inserted into the chorioid coat opposite the ciliary processes. The inner portion of the muscle is interrupted by bundles of fibers which pursue a circular direction (Fig. 287). They collectively constitute the *annular* or *ring muscle* of Müller. The ciliary muscle in common with the circular fibers of the iris receives its nerve supply direct from the nerve-cells in the ciliary ganglion. Contraction of the ciliary muscle tenses the chorioid coat, and for this reason it is frequently termed the *tensor chorioideæ.*

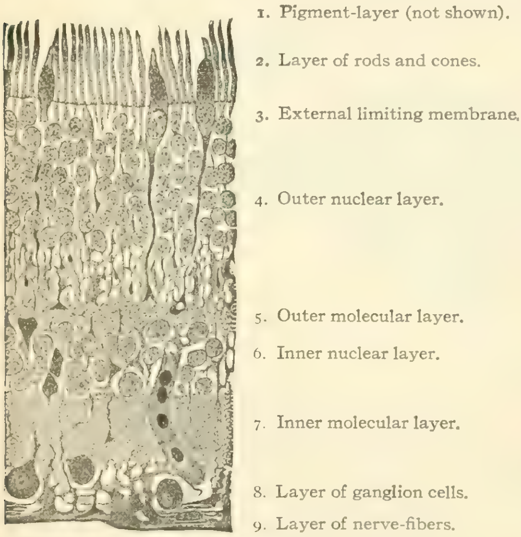
1. Pigment-layer (not shown).
2. Layer of rods and cones.
3. External limiting membrane.
4. Outer nuclear layer.
5. Outer molecular layer.
6. Inner nuclear layer.
7. Inner molecular layer.
8. Layer of ganglion cells.
9. Layer of nerve-fibers.

Fig. 288.—Vertical Section of Human Retina. —(*Schaper.*)

The Retina.—The retina is the internal coat of the eye, extending forward almost to the ciliary processes, where it terminates in an indented border, known as the *ora serrata.* In the living condition it is clear, transparent and pink in color. After death it becomes opaque. The retina is abundantly supplied with blood-vessels, derived from the *arteria centralis retinæ*, a branch of the ophthalmic, which pierces the optic nerve near the sclera, runs forward in its center, to the retina, in which its terminal branches are distributed. The veins arising from the capillary plexus leave the retina by the same route.

In the posterior portion of the retina, at a point corresponding with the axis of vision, there is a small oval area about 2 mm. in its transverse and about 0.8 mm. in its vertical diameter. From the fact that it presents a yellow appearance, it is known as the *macula lutea.* This area presents in its center a depression with sloping sides, known as the *fovea centralis.* About 3.5 mm. to the nasal side of the macula is the point of entrance of the optic nerve.

The retina is remarkably complex in structure, presenting an appearance, when viewed microscopically, something like that represented in Fig. 288, indicating that it is composed of different cellular elements arranged in layers. These have been named, from behind forward, as follows:

1. The layer of pigment cells.
2. The layer of rods and cones, or Jacobson's layer.
3. The external limiting membrane.
4. The outer nuclear or granular layer.
5. The outer molecular or reticular layer.
6. The inner nuclear or granular layer.
7. The inner molecular or reticular layer.
8. The layer of ganglion cells.
9. The layer of nerve-fibers.

Modern histologic methods of research have made it possible to reduce the retina, exclusive of the pigment cells, to three successive layers of nerve-cells, supported by a highly developed neuroglia, forming what has been termed the fibers of Müller. These nerve-cells are as follows:

1. The visual cells.
2. The bipolar cells.
3. The ganglion cells.

The relation of these nerve-cells one to another and to the supporting neuroglia tissue and the manner in which they unite to form the above-mentioned layers are schematically shown in Fig. 289.

The *pigment-layer* is composed of hexagonal cells. Though formerly described as forming a part (the inner layer) of the chorioid, these cells belong embryologically to the retina. From their retinal surface delicate pigmented processes extend into and between the rods and cones. On exposure to light these processess elongate and push themselves between the rods. In the dark they retract and withdraw into the cell-body.

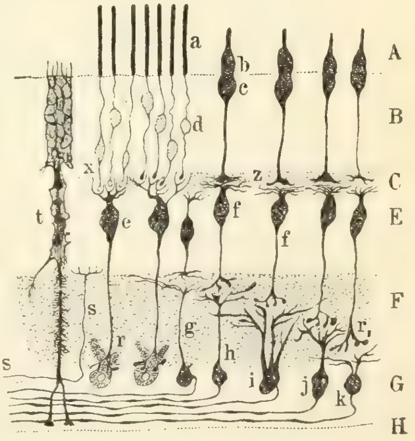

FIG. 289.—CROSS-SECTION OF THE RETINA FROM A MAMMAL. A. Layer of rods and cones. B. Visual cells (outer granules). C. Outer molecular layer. E. Bipolar cells (inner granules). F. Inner molecular layer. G. Ganglion cells. H. Layer of nerve-fibers. a. Rods. b. Cones. e. Bipolar rod. f. Bipolar cone. r. Lower ramification of a bipolar rod. f. Lower ramification of a bipolar cone. g, h, i, j, k. Ganglion cells in various stages, branching from F. x, z. Bipolar contact of rods and cones. t. Müller's supporting fibers. S. Centrifugal nerve-fibers.—(*After Ramón y Cajal.*)

The *visual cells* which form the layer of rods and cones are of two varieties, the rod shaped and the cone shaped.

The rod-shaped visual cell consists of a straight elongated cylinder extending through the entire thickness of Jacobson's membrane and a fine fiber containing a nucleus, which, after piercing the external limiting membrane, passes into the outer molecular layer, where it terminates in a spheric enlargement. The outer portion of the rod is clear and homogeneous, though containing a pigment known as visual purple or rhodopsin; the inner portion of the rod is slightly granular.

The cone-shaped visual cells also consist of two portions, a conic portion situated in Jacobson's membrane between the rods, and a fine fiber, containing a nucleus, which, after piercing the external limiting membrane, passes into the outer molecular layer, where it terminates in a fine tuft. The inner portion of the cone is thicker than the rod and rests on the limiting membrane; the outer portion tapers to a fine point and is known as the cone style. The cones, as a rule, are shorter than the rods. The proportion of rods to cones varies in different parts of the retina, though there are on the average about fourteen rods to one cone. In the macula the rods are entirely absent, cones alone being present.

The layer of visual cells together with the neuroglia constitutes the first of the three layers of the retina proper. The external limiting membrane is formed by the bending of the ends of neuroglia cells.

The *bipolar cells* consist of a central portion, found in the inner nuclear layer, from which are given off two processes which pass in opposite directions, one toward the visual cells, the other toward the ganglion cells. The former terminate in tufts which arborize around the tufts and spheric enlargements of the visual cells, and assist in the formation of the outer molecular layer; the latter terminate in similar tufts in the inner molecular layer.

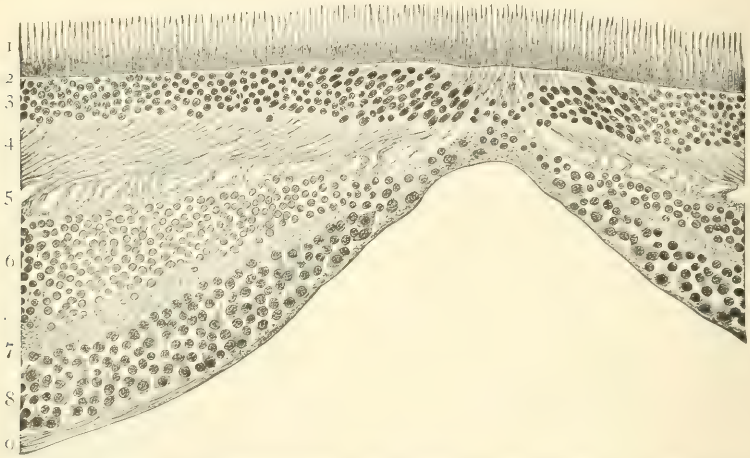

Fig. 290.—Horizontal Section through the Macula and Fovea of a Man Sixty Years Old. The section is not through the exact center of the fovea, for there are only cone visual cells and no remnants of the confluence of the inner granule and ganglion cell layers are present. 1. Cones. 2. External limiting membrane. 3. Outer nuclear layer. 4. Henle's fiber layer. 5. Outer molecular or reticular layer. 6. Inner nuclear layer. 7. Inner molecular or reticular layer. 8. Layer of ganglion cells. 9. Nerve-fiber layer.—(*After Schaper, Stöhr's "Histology."*)

The *ganglion cells* are arranged in a single layer, as a rule. They are large and nucleated. From the inner side of each cell there is given off a single axon which passes toward the center of the retina (forming the nerve-fiber layer), where it enters and assists in forming the optic nerve. From the outer side of the ganglion cell dendrites pass into and assist in forming the inner molecular layer. These dendrites come into physiologic relation with those of the inner processes of the bipolar cells.

Horizontally disposed nerve-cells are also present in the outer molecular layer in relation with the visual cells. Spongioblasts or amacrine cells are also present at the border of and in the inner molecular layer.

From the relation of the ganglion cells, in which the optic nerve-fibers take their origin, to the visual cells and the bipolar cells, the former may be regarded as the *terminal visual organ*, the intermediary between the ether vibrations and the ganglion cell. The visual cells are directed toward the chorioid, away from the entering light, dipping into the pigment cells. They, with the pigment-layer, are the elements by which the ether vibrations are transformed into nerve energy.

In the fovea most of the retinal elements are wanting or are reduced in thickness. The cones alone are present. The cone-fibers with their nuclei are directed obliquely upward and outward along the slope of the fovea, to end in tufts which come into physiologic relation with the dendrites of the ganglion cells, which at the top of the fovea are generally increased in number (Fig. 290).

It is estimated that the optic nerve contains about 500,000 nerve-fibers, and that for each fiber there are about 7 cones, 100 rods, and 7 pigment cells. In accordance with this estimate there would be about 3,500,000 cones, 50,000,000 rods, and 3,500,000 pigment cells. The distance between the centers of two adjacent cones in the fovea is 4 micromillimeters.

The Refracting Media.—The refracting media enclosed by the foregoing membranes are the aqueous humor, the lens and the vitreous humor.

The Aqueous Humor.—The aqueous humor is small in amount in comparison with the vitreous and is found in the space bounded by the cornea, the ciliary body, the suspensory ligament, and the lens. The projection of the iris into this space partially divides it into an anterior and a posterior portion or chamber. The aqueous humor is a clear, watery, alkaline fluid derived from or secreted by the capillary blood-vessels of the ciliary body. From this origin it passes through the pupil into the anterior chamber. It serves to keep the cornea tense and smooth. The ocular tension depends partly on the presence of this fluid in the eyeball. There is every reason for believing that there is a constant stream of fluid from the blood-vessels into the eye and from the eye through the spaces of Fontana at the base of the iris into the canal of Schlemm, and so into the blood. Any interference with the exit of this fluid rapidly increases the intra-ocular tension. Inasmuch as the aqueous humor has the same refracting power as the cornea the two may be regarded as a single body.

The Lens.—The lens is the transparent biconvex body situated just behind the iris, in the concavity of the vitreous. The thickness of the lens is 3.6 mm., the diameter about 9 mm. It consists of a transparent capsule containing elongated hexagonal fibers which, having their origin near the anterior central portion of the lens, pass out toward the margin, where they bend around to terminate in a triradiate figure on the opposite side. Chemically the lens consists of water, a globulin body (crystallin), and salts.

The lens is held in position by the suspensory ligament, formed in part by the hyaloid membrane and in part by fibers derived from the ciliary processes. The former becomes attached to the posterior surface, the latter to the anterior surface of the lens near the equator. The space between the two layers of the ligament is the canal of Petit. The anterior surface of the ligament presents a series of plications conforming to corresponding plications on the surface of the ciliary processes.

The Vitreous Humor.—The vitreous humor is the largest of the refracting media and occupies by far the largest portion of the interior of the eyeball. From its position it gives support to the retina. Anteriorly it presents a concavity, in which the crystalline lens is lodged. The vitreous humor consists of water (97 per cent.), organic matter and salts, enclosed in a transparent membrane, the *tunica hyaloidea*. The mass of the vitreous humor is penetrated by a species of connective tissue.

These bodies, the cornea and aqueous humor, the lens and the vitreous humor, together form a refracting system by which parallel rays of light, which enter the eye when it is in repose, are converged and brought to a focus on the retina.

The relations of the parts entering into the structure of the eye are shown in Fig. 286.

THE PHYSIOLOGY OF VISION

The Retinal Image.—The general function of the eye is the formation of images of external objects on the free ends of the percipient elements of the retina, the rods and cones. The existence of an image on the retina can be readily seen in the excised eye of an albino rabbit, when placed between a lighted candle and the eye of an observer. Its presence in the human eye can be demonstrated with the ophthalmoscope. It is this image, composed of focal points of luminous rays, that stimulate the rods and cones, which is the basis of our sight perceptions, and out of which the mind constructs space relations of external objects. In only two essential respects as far as space relations go, does the image on the retina differ from the appearance of the object, aside from the fact that the object has usually three, the image only two, dimensions—viz., in size and position. Whatever the distance, the image is generally smaller than the object; it is also reversed, the upper part of the object becoming the lower part of the image, and the right side of the object the left side of the image.

The Dioptric or Refracting Apparatus.—The formation of an image is made possible by the introduction of a complex refracting apparatus consisting of the cornea, aqueous humor, lens, and vitreous humor. Without these agencies the ether vibrations would give rise only to a sensation of diffused luminosity. Rays of light emanating from any one point—that is, homocentric rays—arriving at the eye must traverse successively the different refracting media. In their passage from one to the other, they undergo at the surfaces changes in direction before they are finally converged to a focal point. In order to follow mathematically the rays in all their deviations through the media, to determine their focal points and to construct an image, a knowledge of the form of the refracting surfaces, the refractive indices of the different media, and the distance of the surfaces from one another must be known.

The following constants are now accepted: The radius of curvature of that portion of each refracting surface used for distinct vision is for the cornea 7.829 mm., for the anterior and posterior surfaces of the lens 10 and 6 mm., respectively. The indices of refraction of the different media are as follows: cornea and aqueous humor, 1.3365; lens, 1.4371; vitreous body, 1.3365. The distance from the vertex of the cornea to the lens is 3.6 mm.; the thickness of the lens, 3.6 mm.; the distance from the posterior surface of the lens to the retina, 15 mm. As the two surfaces of the cornea are practically parallel, and as the index of refraction of the aqueous humor is the same as that of the cornea, they may be regarded as but one medium. The refracting surfaces may, therefore, be reduced to the anterior surface of the cornea, the anterior surface of the lens, and the posterior surface of the lens.[1]

Parallel rays of light entering the eye pass from air, with an index of refraction of 1.00025, into the cornea, with an index of refraction of 1.3365. In passing from the rarer into the denser medium they undergo refraction in accordance with the laws of optics and are rendered somewhat convergent. The extent of this first refraction and convergence is sufficiently great to bring parallel rays, if continued, to a focus about 10 mm. behind the retina. This would be the condition in aphakia whether the lens is congenitally absent or has been removed by surgical procedures. Perfect vision, however, requires that the convergence of the light must be great enough to bring the focal point, the image, on the retina. This is accomplished by the introduction of an additional refracting body, the lens. On entering the lens the rays are for the same reason—*i.e.*, the passage from a rarer into a denser medium—again refracted and converged, and if continued would come to a focus about 6.5 mm. behind the retina. On passing from the lens into the vitreous—*i.e.*, from a denser into a rarer medium—the rays are once more converged and to an extent sufficient to focalize them on the retina (Fig. 291).

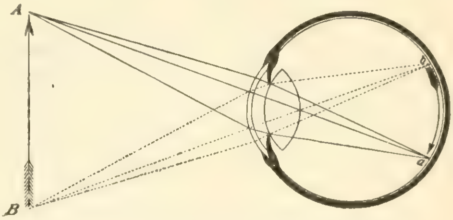

FIG. 291.—REFRACTION OF HOMOCENTRIC RAYS AND THE FORMATION OF AN IMAGE.

While it is thus possible to follow the rays geometrically through these media by means of the above-mentioned factors, the procedure is attended with many difficulties. Moreover, as the relations all change when rays enter the eye from objects situated progressively nearer the eye, a separate calculation is necessitated for each distance for the determination of the size of the image.

A method by which these difficulties are much reduced was suggested by Gauss and developed by Listing. It was demonstrated by Gauss that in every complicated system of refracting media separated by centered spheric surfaces there may be assumed certain *ideal* or *cardinal points*, to which the system may be reduced, and which, if their relative position and properties be known, permit of the determination, either by calculation or geometric construction, of the path of the refracted ray, and the position and size of the image in the last medium, if those of the object in the first medium be known.

Every dioptric system can be replaced, as Gauss showed, by a single system composed of six cardinal points and six planes perpendicular to the common axis—*e.g.*, two focal points, two principle points, two nodal points, two focal planes, two principal planes, and two nodal planes.

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[1] Strictly speaking, the posterior surface of the cornea is not parallel to the anterior surface, and the index of refraction of the cornea is a trifle greater than that of the aqueous humor, viz.: 1.377. But as the increase in the corneal refraction due to the higher index is almost exactly counteracted by a decrease in refraction due to the higher curvature of the posterior corneal surface, the usual assumptions furnish quite accurate results.

Properties of the Cardinal Points.—The *first focal point*, F_1, in Fig. 292, has the property that every ray which before refraction passes through it, after refraction is parallel to the axis.

The *second focal point*, F_2, has the property that every ray which before refraction is parallel to the axis, passes after refraction through it.

The *second principal point*, H_2, is the image of the *first*, H_1; that is, rays in the first medium which go through the first principal point pass after the last refraction through the second. Planes at right angles to the axis at these points are *principal planes.* The second principal plane is the image of the first. Every point in the first principal plane has its image after refraction at a corresponding point in the second principal plane at the same distance from the axis and on the same side.

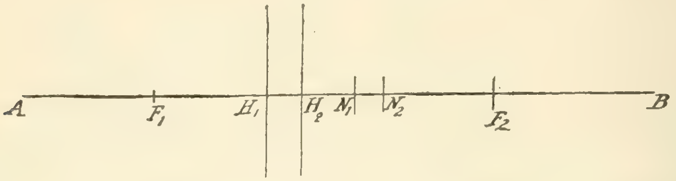

FIG. 292.—DIAGRAM SHOWING THE POSITION AND RELATION OF THE CARDINAL POINTS.

The *second nodal point*, N_2, is the image of the *first*, N_1: a ray which in the first medium is directed to the first nodal point passes after refraction through the second nodal point, and the direction of the rays before and after refraction are paralled to each other. In Fig. 292 let A B represent the axis. The distance of the first focal point, F_1, from the first principal plane, H_1, is the *anterior focal distance.* The distance of the second focal point, F_2, from the second principal plane, H_2, is the *posterior focal distance.* The distance of the first nodal point, N_1, from the first focal point, F_1, is equal to the posterior focal distance H_2 F_2. The distance of the second nodal point, N_2, from the second focal point, F_2, is equal to the anterior focal distance, H_1 F_1. It is evident, therefore, that the distance of the corresponding principal and nodal points from each other is equal to the differences between the two focal distances. Also the distance of the two principal points from each other is equal to the distance of the two nodal points from each other. Finally, the focal distances are proportional to the

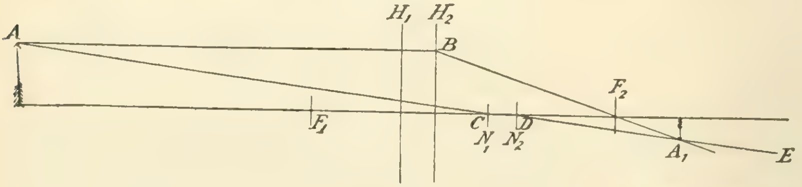

FIG. 293.—DIAGRAM TO FIND THE IMAGE IN LAST MEDIUM OF A LUMINOUS POINT IN THE FIRST.

refractive indices of the first and last media. Planes passing through the focal points vertically to the axis are known as *focal planes*.

From these properties of the cardinal points the position of an image in the last medium of a luminous point in the first may be determined, and the course of a refracted ray in the last medium be constructed if its direction in the first be given according to the following rules:

1. To find the image in the last medium of a luminous point in the first: Let A (Fig. 293) be this given point. Draw $A B$ parallel to the axis until it meets the second principal plane in B; then $B F_2$ will be this ray after refraction. Draw a second ray from A to the first nodal point; then draw another ray, $D E$, from the second nodal point parallel to $A C$. This will be the refracted ray in the last medium. Where the two refracted rays, BF_2 and $D E$, intersect, the image of A will be A_1.[1]
2. To find the refracted ray in the last medium of a given ray in the first medium: Let $A B$ (Fig. 294) be the given ray. Continue this ray until it meets the first principal plane in C. Draw $C D$ parallel to the axis. Now assume any point, such as E, in the given ray, and find its image E_1 by the Rule 1. Then $D E_1$ becomes the course of the refracted ray.

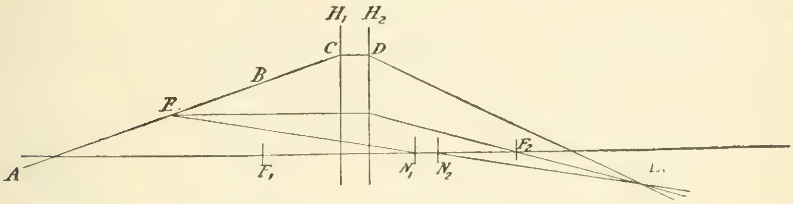

FIG. 294.—DIAGRAM TO FIND THE REFRACTED RAY IN THE LAST MEDIUM OF A GIVEN RAY IN THE FIRST MEDIUM.

The Schematic Eye.—Accepting the system of cardinal points, Listing, Donders, and v. Helmholtz have constructed "schematic" eyes to be substituted for the refracting system of the natural eye.

For this purpose it is necessary to make use of the various estimates of the indices of refraction of the different media, of the radii of curvatures of the different refracting surfaces, and of the distances separating them, to deduce an average eye as a basis for calculation. The most widely accepted attempt is that of v. Helmholtz. The data he assumed are as follows: The refractive index of air = 1; of the cornea and aqueous humor, 1.3365; of the lens, 1.4371; of the vitreous humor, 1.3365; the radius of curvature of the cornea, 7.829 mm.; of the anterior surface of the lens, 10 mm.; of the posterior surface, 6 mm.; the distance from the apex of the cornea to the anterior surface of the lens, 3.6 mm.; thickness of lens, 3.6 mm. From the above-mentioned data v. Helmholtz calculated the position of the cardinal points for the eye as follows (see Fig. 295): The first focal point is situated 13.745

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[1] If the point A is infinitely far from the eye, all the rays striking the eye will be parallel to each other. The nodal ray must therefore be drawn, and the point where this nodal ray meets the second focal plane will be the image of A, or A_1 where all rays parallel to the nodal ray will meet.

mm. before the anterior surface of the cornea; the second focal point is situated 15.619 mm. behind the posterior surface of the lens; the first principal point, 1.753 mm. behind the cornea; the second principal point, 2.106 mm. behind the cornea; the first and second nodal points, 6.968 and 7.321 mm. behind the apex of the cornea, respectively. The anterior focal distance of this schematic eye, the distance between F_1 and H_1, therefore amounts to 15.498 mm., and the posterior focal distance, H_2 to F_2, to 20.713 mm.

When the eye, however, is accommodated for near vision, the relations of the cardinal points are changed and will be as follows, if the point accommodated for lies 152 mm. from the cornea: Anterior focal distance, 13.990 mm.; posterior focal distance, 18.689 mm.; distance from cornea of the first and second principal points, 1.858 and 2.257 mm. respectively; distance of the posterior focus, 20.955 mm. from cornea. Given this schematic eye in the accommodated state, the course of the rays and the determination of the position of an image in the last medium of a luminous point in the first can easily be determined by the rules already given.

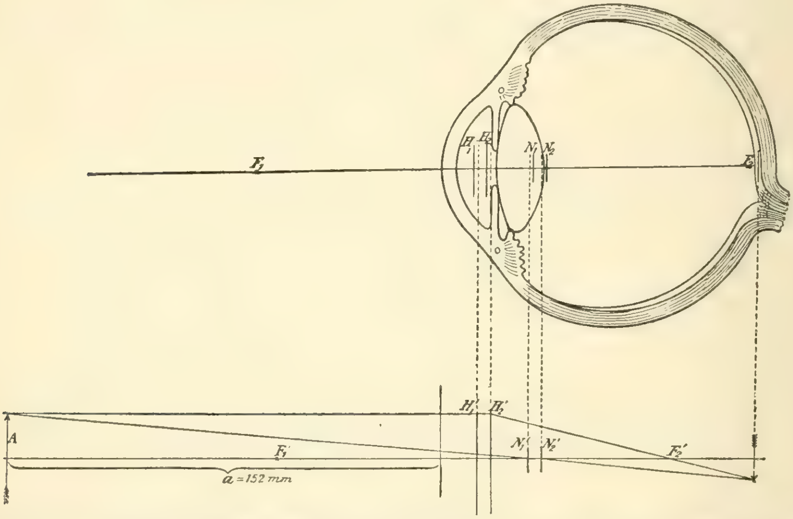

FIG. 295.—DIAGRAM SHOWING THE POSITION OF THE CARDINAL POINTS IN THE "SCHEMATIC EYE." The continuous lines in the upper half of the figure show their position in the passive emmetropic eye. The dotted lines indicate the change in their position in an eye accommodated for the object *A* at the distance *a* from the cornea, or 152 mm. The lower half of the figure shows the formation of a distinct image on the retina of an eye accommodated for the object *A* at the distance *a* from the cornea.

The Reduced Eye.—As suggested by Listing, this schematic eye may be yet further simplified or reduced to a single refracting surface bounded anteriorly by air and posteriorly only by aqueous or vitreous humor. Without introducing any noticeable error in the determination of the size of the retinal image, the anterior principal and the anterior nodal points may be disregarded, owing to the minuteness of the distances (0.39 mm.) separating the two systems of points. There is thus obtained one principal point and one nodal point, which latter becomes the center of curvature of the single refracting surface. The dimensions of this "reduced" eye are as follows (see Fig. 296). From the anterior surface of the cornea, corresponding to the principal plane *H*, to the nodal point *N*, 5.215 mm., from the anterior focal point F_1, to the principal plane *H*, *i.e.*, the anterior focal distance f', 15.498 mm.; from the principal plane *H* to the posterior focal point F_2, *i.e.*, the posterior focal distance f'', 20.713 mm.; the index of refraction is 1.3365. There is thus substituted for the natural eye a single refracting surface with a radius of curvature, *r*, of 5.125 mm. In such an eye luminous rays emanating from the anterior focal point are parallel to the axis after refraction in the interior of the eye. Also rays parallel to the axis before refraction unite at the posterior focal point.

By means of this reduced eye the construction of the refracted ray, the various calculations as to the size of the image, the size of diffusion circles, etc., are greatly facilitated: *e.g.*,

In Fig. 297 let *A B* represent an object. From *A* a pencil of rays falls on the single refracting surface. One of the rays, the nodal ray, falling on the surface perpendicularly, passes unrefracted through the single nodal point, *N*, to the posterior focal plane. The remaining rays, partially represented in the figure, falling on this surface under varying degrees of incidence, undergo corresponding degrees of refraction, by which they form a converging cone of rays which unite at a point situated on the nodal ray. These two points, *A*, *a*, are known as *conjugate foci.* The same holds true for a pencil of rays emanating from *B* or any other point of the object.

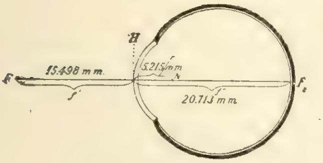

FIG. 296.—THE REDUCED EYE.

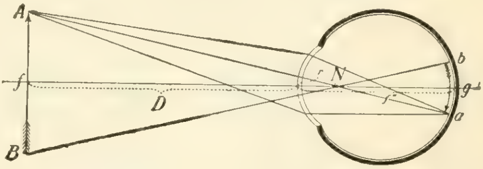

FIG. 297.—THE FORMATION OF AN IMAGE IN THE REDUCED EYE.

The Size of the Retinal Image.—The size of the retinal image, *I* (in Fig. 297 *a b*), may now be easily calculated, when the size of the object, *O* (in Fig. 297 *A B*), and its distance, *D*, from the refracting surface with radius of curvature, r, are known, by the following formula:

$$O : I = D + r : f'' - r.$$

For, as the triangles *A N B* and *a N b* are similar, we have

$$A\,B : a\,b = f\,N : N\,g, \text{ or } a\,b = \frac{A\,B \times N\,g}{f\,N}; \text{ and therefore } I = \frac{O(f'' - r.)}{D + r}$$

Independent of the foregoing method, the size of the retinal image may be calculated if it is remembered that the eye, like any optic system, has a point of such a quality that a ray of light which before entering the eye was directed toward it, after refraction continues as if it came from this point. In other words, there is in the eye a point which allows a ray of light to pass unrefracted as would a pinhole instead of a lens. This point, termed the nodal point of the eye, determines the size of the image; for if a line be drawn from both the upper and lower ends of an object through this nodal point, it is clear that the images of the respective points must lie on these two rays where they intersect the retina. The distance of this nodal point from the retina is 15.498 mm. It is clear, therefore, that the size of the object is to the size of the image, as the distance of the object from the nodal point is to the distance of the nodal point from the retina; or, in other words, to find the size of the retinal image: multiply the diameter of the object by 15.5 mm. and divide by the distance of the object from the eye.

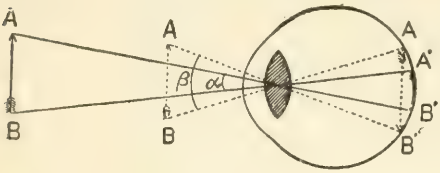

Fig. 298.—Drawing Designed to show how the Visual Angle and Size of Retinal Image Varies with the Distance of an Object of Given Size. For the distant position of A–B the visual angle is a; for the near position (dotted lines) β.—(*From Stewart.*)

The Visual Angle.—The visual angle is defined as the angle formed by the intersection of two lines drawn from the extremities of an object to the nodal point of the eye. Beyond the nodal point, however, the lines again diverge and form an inverted or reversed image of the object on the retina. The size of the visual angle increases with the nearness and decreases with the remoteness of the object; the retinal image correspondingly increases and decreases in size. These facts will become apparent from an examination of Fig. 298. As the size of the retinal image diminishes when the visual angle diminishes either as a result of the removal of a given object from the eye, or of a diminution of the size of the object, there comes a limit in the size of the visual angle, beyond which it is impossible to see the two end points (*A* and *B*) of the object separately. When this limit is reached the size of the angle expressed in degrees of the circle, may be determined if the distance between the two points and their distance from the eye be known. Thus it has been experimentally determined that at a distance of 5 meters, the smallest object or the smallest interval between two points which permits the eye to distinguish them as such, is about 1.454 mm. Lines drawn from the extremities of such an object or interval, to the nodal point, subtend an angle of 60 seconds.[1] Beyond this the two points are indistinguishable. In other words the emmetropic eye possesses the power of distinguishing the correspondingly

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[1] The size of the visual angle, under which an object of this size and situated at a distance of 5 meters is distinctly seen, can be determined from the following Fig. 316, in which *A B* represents the size of the object 1.454 mm.; *N*, the nodal point; *CN*, the line which bisects the object, represents the distance of the object from the nodal point; *a*, the visual angle subtended and whose value it is desired to know, and *b* one-half of the angle *a*. By trigonometry the size of the angle *a* can be determined in the following way: one-half the size of the object *A B*, is divided by its distance from the nodal point; the quotient is the tangent of half the angle. Thus 0.727 ÷ 5000 = 0.0001454. By reference to tables of natural tangents, it will be found that the angle or fraction of the circle corresponding to this tangent is 30 seconds, and that therefore the whole angle is 60 seconds.

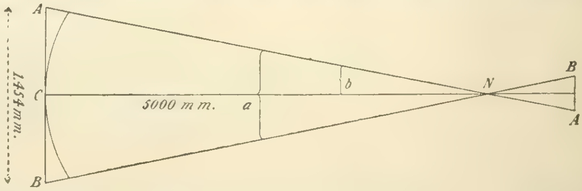

Fig. 209.—Figure showing the Method of Obtaining the Visual Angle Expressed in Degrees or Fraction of a Degree of an arc.

small interval between the two images on the retina of the two objective points. The size of the image or the interval between the two retinal points, determined from the foregoing factors by the formulæ on page 692 is 0.004 mm., which would correspond to a visual angle of 60 seconds. If the retinal distance is less than this the two sensations fuse into one. The reason assigned for this is, that the distance between the centers of two adjoining cones in the macula is 0.004 mm. With a visual angle not less than 60 seconds, the two foci fall on separate cones. With a smaller visual angle the two foci fall on, and excite but a single cone and hence there arises the sensation of but a single point. The acuteness of vision, therefore, of the emmetropic eye depends on its power of distinguishing the smallest retinal image or the smallest interval between two cones on the retina, corresponding to a visual angle of 60 seconds.

In ophthalmic practice it is customary in testing the acuteness of vision to employ test letters of specific sizes for specific distances. The letters are so proportioned that when they are placed at the specified distances, the extremities of the letters subtend an angle of 5 minutes. The letters have been constructed on the following basis: Since to an angle of 60 seconds there corresponds an object of 1.454 mm. at the distance of 5 meters as shown before and as the object decreases in proportion to the distance (for the same visual angle) it is evident that the object would have to be one-fifth of 1.454 mm. or 0.2908 mm. in order to subtend an angle of 60 seconds at one meter. From this the size for any other distance in meters is found simply by multiplying 0.2908 mm. by the distance. The standard letters are so constructed that each is inscribed within a square, the sides of which at a specific distance, 5 meters, subtend an angle of 5 minutes and which is again subdivided into 25 small squares each side of which subtends an angle of 1 minute. These partial little squares correspond to the details of the letter while the whole letter of course, embraces an angle of 5 minutes both as to height and to breadth (Fig. 300). The letter that could be distinctly seen at a distance of 5 meters, would have, therefore, a vertical and a horizontal dimension of 5 times 1.454 mm. or 7.27 mm. (Fig. 300 A), and at 10 meters corresponding dimension of 14.54 mm., etc. (Fig. 300 B.)

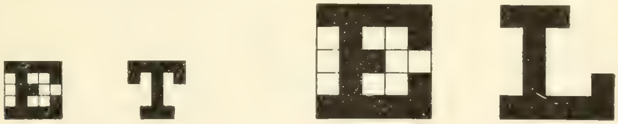

FIG. 300.—STANDARD LETTERS, FOR TESTING THE ACUITY OF VISION.

If with the accommodation suspended, the emmetropic eye could clearly distinguish at a distance of 5 meters a letter 7.27 mm. in size which would, therefore, subtend an angle of 5 minutes, then the acuity of the vision would be normal and could be expressed as follows: $V = \frac{5}{5}$ or $V = 1$. If on the contrary at this distance the smallest letter that could be clearly seen is one that would subtend an angle of 5 minutes at a distance of 10 meters then the visual acuity would be only one-half the normal and could be expressed as follows: $V = \frac{5}{10}$ or $V = \frac{1}{2}$, etc. The acuity of vision is expressed, therefore, by a fraction the numerator of which is the distance at which the test is made and whose denominator is the distance at which the smallest letters distinguished by the patient subtend an angle of 5 minutes, or in other words the distance at which the patient reads divided by the distance at which he ought to read the smallest letters seen by him on the chart.

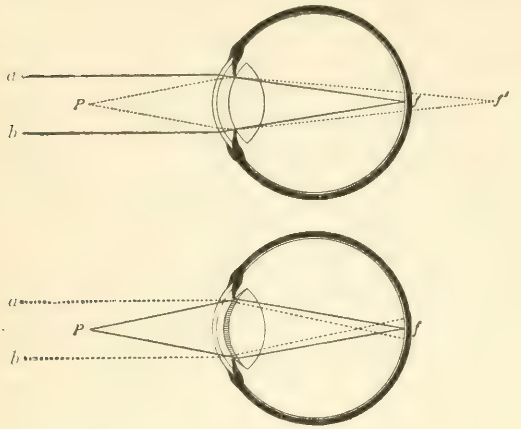

FIG. 301.—THE REFRACTION OF PARALLEL AND DIVERGENT RAYS IN THE EMMETROPIC EYE IN THE PASSIVE AND IN THE ACTIVE OR ACCOMMODATED CONDITION.

Accommodation. — Accommodation may be defined as the power which the eye possesses of adjusting itself to vision at different distances; or in other words, the power of focusing rays of light on the retina, which come from different distances at different times. That such a power is a necessity is apparent from the fact that it cannot focus rays coming from a distant and a near object at the same time. Thus, if an object is held before one eye at a distance of 22 centimeters, for example, and the vision is directed to a distant object it is evident that the near object is indistinctly seen; but if the vision is then directed to the near object, it in turn becomes clear and distinct, while the distant object becomes blurred and indistinct. It is evident, therefore, that rays of light coming from a distant and a near object cannot be simultaneously, but only alternately, focused on the retina. The observer at the same time becomes conscious, as the vision is directed from the distant to the near object, of a change in the eye itself, a change that involves time and effort. The reasons for these facts will become apparent from a consideration of the following facts:

In a normal or *emmetropic* eye, parallel rays of light (Fig. 301, *a*, *b*) after passing through the optic media are converged and brought to a focus on the retina, *f*. Rays, however, which come from a luminous point situated near the eye, *P*, and are therefore divergent, passing through the optic media at the same time, are intercepted by the retina before they are focused, and give rise to the formation of *diffusion-circles* and indistinctness of vision. The reverse is also true. When the eye is adjusted for the refraction and focusing of divergent rays (Fig. 301, *P*) parallel rays will be brought to a focus before reaching the retina, and, again diverging, will form diffusion-circles. It is evident, therefore, that it is impossible to focus simultaneously both parallel and divergent rays, and to see distinctly at the same time, two objects which are situated at different distances. The eye must be alternately adjusted first to one object and then to another. To this adjustment the term accommodation has been given.

The following table of Listing shows the size of the diffusion-circles formed of objects situated at different distances when the accommodative power is suspended in an emmetropic eye:

Distance of Luminous Point.	Distance of the Focal Point behind the Posterior Surface of the Retina.	Diameter of the Diffusion-circle.
∞	0.0 mm.	0.0 mm.
65 m.	0.005 mm.	0.0011 mm.
25 m.	0.012 mm.	0.0027 mm.
12 m.	0.025 mm.	0.0050 mm.
6 m.	0.050 mm.	0.0112 mm.
3 m.	0.100 mm.	0.0222 mm.
1.500 m.	0.20 mm.	0.0443 mm.
0.750 m.	0.40 mm.	0.0825 mm.
0.375 m.	0.80 mm.	0.1616 mm.
0.188 m.	1.60 mm.	0.3122 mm.
0.094 m.	3.20 mm.	0.5768 mm.
0.088 m.	3.42 mm.	0.6484 mm.

From the foregoing table it is evident that between infinity and 65 meters, the diffusion-circles are so slight that no perceptible accommodative effort is required to eliminate them. From 65 meters to 6 meters the diffusion-circles gradually become larger, though they are yet so faint as to require for their correction an accommodative effort which is scarcely measurable. From 6 meters up to 6 centimeters, however, a progressive increase in accommodative power is demanded for distinct vision.

The normal eye when adjusted for distant vision is in a passive condition, and hence vision of distant objects is unattended with fatigue. In the act of adjustment, however, for near vision the eye passes into an active state, the result of a muscle effort, the energy of which is proportional to the nearness of the object toward which the eye is directed.

Mechanism of Accommodation.—Inasmuch as neither the corneal curvature nor the shape of the eyeball undergoes any change during accommodation, the necessary change, whatever it may be, is to be sought for in the lens. As to the character of the changes in this body, two views are held, based largely on the fact and its interpretation, that images of a luminous point reflected from the anterior surface of the cornea and the anterior and posterior surfaces of the lens, change their relative positions during accommodation.

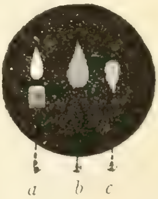

Fig. 302.—Catoptric Images in the Eye. *a.* Upright image of reflection, from the cornea. *b.* Upright image from the anterior surface of the lens. *c.* Inverted image, from the posterior surface of the lens.—(*Helmholtz.*)

Thus, if in a darkened room a lighted candle be placed in front of and to the side of an individual whose eye is directed to a distant object, an observer placed in the same relative position as the candle will observe three images in the eye, one at the surface of the cornea and two at the pupillary margin (Fig. 302). Of the two latter, one is quite large and situated apparently in front of the third, which is faint, small, and inverted. The middle image is reflected from the anterior surface of the lens, the last from the posterior surface. These images of reflection are known as *catoptric* images. If now the individual be directed to fix the gaze on a near object, the second image changes its position, advances toward the corneal image and at the same time becomes smaller, a change which, in accordance with the laws of optics, could only be due to an increase in the convexity of the anterior surface of the lens. A slight displacement of the third image sometimes observed indicates a possible increase in the convexity of the posterior surface of the lens.

According to Helmholtz, during accommodation the entire anterior surface of the lens becomes more convex, while at the same time it slightly advances, possibly as much as 0.4 mm. in extreme efforts. This change is represented in Fig. 303. According to Tscherning, the increase in convexity of the anterior surface is confined to the central portion, the remainder of the surface becoming somewhat flattened. There is, moreover, no evidence that there is any advance of the surface or any increase in the thickness of the lens. A series of new and ingenious experiments lend support to Tscherning's view, though of late Hess has brought forward definite experimental evidence in favor of the view of Helmholtz. The radius of curvature in either case approximates 6 mm. in extreme efforts of accommodation. The increase in convexity naturally increases the refracting power.

Whichever view is accepted, the nearer the object—that is, the greater the degree of divergence of the light rays—the more pronounced must be the increase in convexity in order that they may be sufficiently converged and focalized on the retinal surface. Changes in the convexity of the lens, either of increase or decrease, are attended by changes in the distinctness of images. Coincidently with the lens change, the pupillary margin advances and the pupil itself becomes smaller. By this means an indistinctness of the image is prevented by cutting off the rays which would give rise, owing to the angle at which they fall on the surface, to diffusion-circles, from spheric aberration.

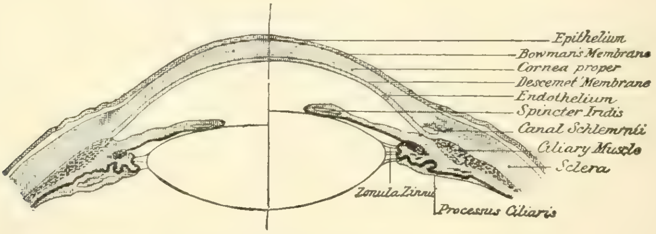

FIG. 303.—THE LEFT HALF REPRESENTS THE EYE IN A STATE OF REST. THE RIGHT HALF IN STATE OF ACCOMMODATION.

The Function of the Ciliary Muscle.—Though it is generally admitted that the increase in the convexity of the lens is caused by the contraction of the ciliary muscle, the exact manner in which this is accomplished is not clearly understood. According to Helmholtz, when the eye is in repose and directed to a distant object the lens is somewhat flattened from a traction exerted by the suspensory ligament. When the eye is directed to a near object, the ciliary muscle contracts, thereby relaxing the ligament, as a result of which the lens, by virtue of an inherent elasticity, bulges forward and becomes more convex. In consequence of this latter fact the refracting power is proportionally increased. In extreme efforts of accommodation it is believed by some observers that the circularly arranged fibers, the so-called annular muscle, contract and exert a pressure on the periphery of the lens and thus aid other mechanisms in relaxing the ligament and in increasing the convexity. This view appears to be supported by the fact that in hypermetropia, where a constant effort is required to obtain a distinct image of even distant objects, the annular muscle becomes very much hypertrophied, thus reinforcing the meridional fibers. In myopia, on the contrary, where the accommodative effort is at a minimum, the entire muscles possesses less than its average size and development.

According to Tscherning, a different explanation of the action of the ciliary muscle must be given. Thus, when it contracts, the antero-internal angle, that portion in close relation with the suspensory ligament, recedes and exerts on the ligament a pressure which in turn exerts a traction on the peripheral portions of the anterior surface of the lens, which produces the deformation observed. At the same time the postero-external portion of the muscle exerts traction on the chorioid, thus sustaining the vitreous and indirectly the lens.

The reason for the flattening of the periphery of the lens from zonular compression and the sharpening of the central convexity is to be found in the fact that the convexity of the more solid central portion, the nucleus, is greater than that of the lens itself. Hence it is easily understood why a zonular traction would give rise to peripheral flattening.

There is, however, one point which seems difficult to harmonize with Tscherning's view; that is, the fact that during accommodation the lens appears to be slightly tremulous, thus showing relaxation, and not increased tension, of the suspensory ligament.

Range of Accommodation.—It has been stated that rays of light coming from a luminous point situated at any distance beyond 65 meters are so nearly parallel that no accommodative effort is required for their focalization. So long as the luminous point remains between infinity and 65 meters, the eye, directed toward it, remains completely relaxed. The point at which the object can be distinctly seen without accommodation is termed the far point or the *punctum remotum.* This for the normal eye is at a distance of 65 meters or beyond.[1] If the luminous point gradually approaches the eye from a point 65 meters distant, the accommodative power comes into play and gradually increases until it attains its maximum. The nearest point up to which the eye is able to form distinct images of objects is called its near point or *punctum proximum.* This near point in a healthy boy of twelve years will lie at a point situated 7 cm. from the eye, while the same point lies 20 cm. distant in a man of forty years. Of objects which lie nearer than the punctum proximum the eye cannot form distinct images. The distance between the *punctum remotum* and the *punctum proximum* is termed the *range of accommodation.*

Force of Accommodation.—The increase in curvature of the lens necessary to focalize rays when the eye is directed from the far to the near point necessitates the expenditure of energy on the part of the ciliary muscle. The force expended in the act of accommodation may be measured by a lens, the refracting power of which is such as to enable it to produce the same result—that is, to give the diverging rays coming from the near point, *e.g.*, 20 cm., a parallel direction. A lens, therefore, which has a focal distance of 20 cm. would be a measure of the force expended; for such a lens placed in front of the *crystalline* lens, when in a state of repose, would, with the assistance of the latter, bring diverging rays coming from the near point to a focus on the retina. A lens of this character is said to have a refracting power of 5 dioptries.[1]

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[1] In practical ophthalmic work a point six meters distant is taken as the far point for the reason that the rays at this distance are practically parallel.

The refracting media of the human eye in *repose* have collectively a refracting power of about 64 dioptries, the reciprocal of its anterior focal distance. The refracting power of the corneal surface alone is equivalent to 42 dioptries. The crystalline lens by reason of its relations and situation in the optic media has a refracting power of about 20 dioptries.

The capability of the lens to increase its refraction during accommodative efforts beyond the 20 dioptries varies considerably at different periods of life. From youth to old age, the elasticity of the lens steadily declines, and the range of accommodation diminishes from the recession of the near point.

The following table shows the decrease in the accommodative power with increasing years, the shortening of the range of accommodation and the distance to which the near point has receded from the eye.

Age, Years	Range of Accommodation, Dioptries	Near point, cm.
10	14.0	7.0
20	10.0	10.0
30	7.0	14.0
40	4.5	22.0
45	3.5	28.0
50	2.5	40.0
60	1.0	100.0
70	Zero	Zero

Convergence of the Eyes during Accommodation.—When the eyes are at complete rest and directed to some far distant object the visual lines are parallel and the optic axes are directed outward at an angle of about 5 degrees, which is known as the angle alpha. If, however, it is desired to see distinctly with both eyes, any object within the range of accommodation, the eyeballs must be converged toward the median line, the object being to enable the rays of light emanating from a point to fall directly into the foveæ so that the two retinal images shall give rise to but a single impression and thus prevent double vision or diplopia which would otherwise result. Convergence of the eyeballs, therefore, increases as the visual axes are directed toward objects which are placed progressively nearer the eyeballs. This is accomplished by the conjoint and harmonious action of the internal recti muscles balanced by the action of their physiologic antagonists—the external recti muscles. Convergence of the eyeballs is always accompanied by increase in the accommodation, the two being necessary for distinct binocular vision.

Functions of the Iris.—For purposes of distinct vision it is essential that the quantity of light entering the interior of the eye shall be so adjusted that the formation and subsequent perception of the image shall be sharp and distinct. This is accomplished by the iris, the circular fibers of which respectively contract and relax with increasing and decreasing intensities of the light. The size of the pupil, therefore, through which the light passes, will vary from moment to moment and in accordance with variation in the light intensity. The quantity of light necessary to distinct vision is thus regulated.

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[1] Since lenses of the same curvature made from different materials have different refracting powers, it becomes necessary to have, for purposes of comparison, some unit of measurement. The unit now accepted is the refracting power of a glass lens which is sufficient to focalize parallel rays at a distance of 100 cm. or 1 meter. This amount of refracting power is termed *a dioptry*. Lenses which would focalize parallel rays at a distance of 50, 20, or 10 cm. are said to have a refractive power of 2, 5, 10 dioptries respectively, obtained by dividing 100 cm. by the focal distance. The refracting power of a biconcave lens is determined by prolonging backward in the direction the parallel rays have come, the rays which have been rendered divergent by the lens, and using a corresponding negative figure. Thus a lens which diverges parallel rays in such a way as to make them appear to radiate from a point 20 centimeters behind itself is said to have a refractive power of *minus* 5 dioptries.

In the total absence of light the sphincter pupillæ muscle is relaxed and the pupil widely dilated. With the appearance of light and an increase in its intensity the muscle again contracts and the pupil progressively narrows. With a given intensity in the light, the sphincter contraction is greater when the light falls directly upon the fovea. Contraction of this muscle is an associated movement in the convergence of the eyes during accommodation and in consensus with the other eye.

In addition to this function of the iris, it constitutes, by virtue of the sphincter muscle contraction, an important corrective apparatus. Being non-transparent, it serves as a diaphragm intercepting those rays which would otherwise pass through the peripheral portions of the lens and by spheric aberration give rise to indistinctness of the image. The movements of the iris by which the size of the pupil is determined are caused by the contractions and relaxations of the *sphincter pupillæ* and *dilatator pupillæ* muscles. The contraction of the sphincter is entirely reflex and involves those structures necessary to the performance of any reflex act, viz.: a receptive surface, the retina; afferent nerves, the pupillary fibers of the optic nerve; a central emissive center situated in the gray matter beneath the aqueduct of Sylvius; and efferent nerves, the motor oculi and the ciliary nerves. The stimulus requisite to the excitation of this mechanism is the impact of light waves or ether vibrations on the rods and cones. According to the intensity of these vibrations will be the resulting contraction of the muscle. The contraction of the dilatator pupillæ muscle is determined by the activity of a continuously active nerve-center in the medulla oblongata which transmits its nerve impulses through the spinal cord, along the first and second dorsal nerves to the superior cervical ganglion, and thence to the iris by way of the fifth nerve. (See Fig. 268, page 620.) These two muscles appear to bear an antagonistic relation to each other, for section of the motor oculi is followed by relaxation of the sphincter muscle and dilatation of the pupil. Stimulation of the sympathetic is followed by a more pronounced dilatation. The size of the pupil is the resultant of a balancing of these two forces.

OPTIC DEFECTS

Presbyopia.—Presbyopia may be defined as a condition of the normal eye in which the accommodation has become so reduced by age that reading has become impossible at ordinary distances. As age advances the lens gradually loses its elasticity and hence its power to increase in convexity and thickness to the same extent as in earlier life, in response to efforts of accommodation. The refractive power is, thereby, lessened and the eye is no longer able to see distinctly at the normal reading distances, viz.: 22 to 28 cm. Rays of light emanating from a luminous point at the normal reading distances are less and less converged on the retina and hence the diffusion circles increase in size. The near point, the point from which divergent rays can be focalized, therefore advances toward the far point, or recedes from the individual. The range of accommodation is, thereby, diminished. At forty years the near point is about 22 cm., indicating an increase in refracting power on the part of the lens of 4.5 dioptries; at forty-five years the near point has receded to 28 cm. This indicates that the lens at this period has only a refracting power of approximately 3.5 dioptries, showing therefore a loss in the five years of 1 dioptry; at fifty years the near point recedes to 40 cm., and at sixty to 100 cm., indicating a loss in refracting power on the part of the lens of 2 and 3.5 dioptries respectively. Convex lenses placed before the eyes having a refracting power of 1, 2, and 3.5 dioptries would in the three instances return the near point to its normal position. At the age of seventy the lens is incapable of any increase during an accommodative effort. A lens of 4.5 dioptries would therefore be required by such a man to return the near point to its normal position, 22 cm. from the eye.

Myopia.—Myopia may be defined as a condition of the eye characterized by an increase in the antero-posterior diameter or by a hypernormal refracting power of the lens. The former is the usual condition. In either case parallel rays of light which enter the eye are brought to a focus in front of the retina, after which they diverge and give rise to diffusion circles and indistinctness of vision. Divergent rays, however, which enter the eye are focalized as usual on the retina even in its new position. The distant point, the punctum remotum is always at a finite distance, but approaches the eye as the myopia increases. The near point is usually much nearer the eye than 20 cm. For this reason the condition is termed *near sight* (Fig. 304).

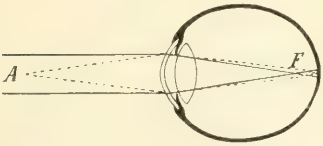

FIG. 304.—MYOPIA. Parallel rays focus at F, cross and form diffusion-circles; divergent rays from A focus on the retina.

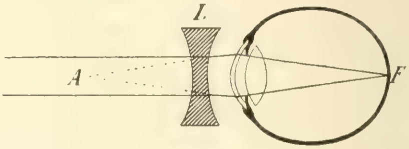

FIG. 305.—CORRECTION OF MYOPIA BY A CONCAVE LENS.

The increase in the length of the antero-posterior diameter may range from a fraction of a millimeter up to 3.8 mm. With an increase of 0.16 mm. the far point is but 200 cm. distant; and with an increase of 3.8 mm. it is but 10 cm. distant. Inasmuch as only divergent rays can be focalized by the myopic eye normal vision can be established by placing before the eyes a biconcave lens with a diverging power in the first instance of 0.5 dioptry and the second of 10 dioptries (Fig. 305).

Hypermetropia.—Hypermetropia may be defined as a condition of the eye characterized by decrease of the normal antero-posterior diameter or by a subnormal refracting power of the lens. The former is the usual condition. In either case parallel rays of light which enter the eye are, therefore, not brought to a focus when the accommodation is suspended. Falling on the retina previous to focalization, they give rise to diffusion-circles and indistinctness of the image. As no object can be seen distinctly no matter how remote, there is no *positive* far point. The near point is abnormally distant—sometimes as far as 200 cm. For this reason the condition is termed *far sight.* A hypermetropic eye without accommodative effort can focalize only converging rays on the retina. If rays of light were to come from the retina of such an eye, they would, on emerging, take a divergent direction, as shown in Fig. 306, dotted line *C* and *D*. If these same rays were to be prolonged backward, they would meet at the point *K*, which is the *punctum remotum;* and as it is behind the eye, it is termed *negative.* Since rays coming from the retina take a divergent direction on emerging from the eye, it is evident that only converging rays can be focalized by a passive hypermetropic eye. The hypermetropic person attempts, and partially succeeds, in focalizing the rays by increasing the convexity of the lens through an increased accommodative effort which often gives rise to accommodation fatigue and headache. As there are no convergent rays in nature, it is necessary for distinct vision that all rays, parallel and divergent, shall be given a convergent direction before entering the eye. The decrease in the length of the antero-posterior diameter may range from a fraction of a millimeter up to 2.78 mm. Normal vision may be established by placing before the hypermetropic eye convex lenses with a converging power, in the first instance, of 0.5 dioptry and, in the second instance, of 10 dioptries (Figs. 307 and 308).

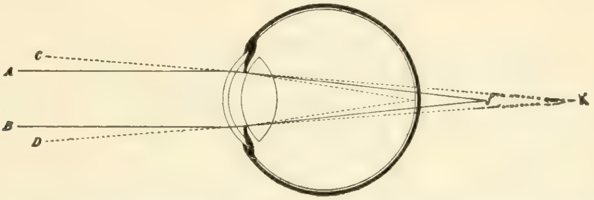

FIG. 306.—THE HYPERMETROPIC EYE. Parallel rays (*A*, *B*) can be focused only at a point behind the eye, as at *f*; rays of light coming from the retina take, on emerging from the eye, a divergent direction, *C*, *D*. *K*. The negative punctum remotum.

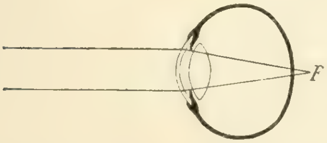

FIG. 307.—HYPERMETROPIA. PARALLEL RAYS FOCUSED BEHIND THE RETINA.

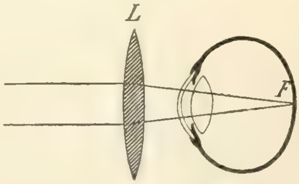

FIG. 308.—CORRECTION OF HYPERMETROPIA BY A CONVEX LENS.

Astigmatism.—Astigmatism may be defined as a condition of the eye characterized by an inequality of curvature of its refracting surfaces in consequence of which not all of a homocentric bundle of rays are brought to the same focus. The inequality may be either in the cornea or lens, or both, though usually in the cornea.

In the normal cornea the radius of curvature in the vertical meridian is a trifle shorter, 7.6 mm., than that of the horizontal, 7.8 mm., and hence its focal distance is slightly shorter. The difference, however, in the focal distances is so slight that the error in the formation of the image is scarcely noticeable. A transverse section of a cone of light coming from the cornea is practically a circle. If, however, the vertical curvature exceeds the normal to any marked extent, the rays passing in the vertical plane will be more sharply refracted and brought to a focus much sooner than the rays passing through the horizontal plane. The result will be that the cone of light will be no longer circular, but more or less elliptic. The variations of the shape of this cone are shown in Fig. 309, which represents the appearance presented on cross-section both before and after focalization of each set of rays. Though the vertical plane has usually the sharper curvature, it not infrequently happens as illustrated in this figure, that the reverse is true. For the reason that the rays from one point do not all come to the same focus or point, the condition is termed astigmatism.

Spheric Aberration.—When the rays of light which emanate from a point fall upon a spheric lens, they do not after passing through it reunite at one point because of the fact that the more peripheral rays have a shorter focus than the central rays. To this condition the term spheric aberration is given. Spheric aberration can be demonstrated in the human eye. That this condition is present to but a slight extent in the normal eye is due to the presence of the iris, which intercepts those rays which would otherwise pass through the marginal portions of the refracting media. In widely dilated eyes the spheric aberration of the peripheral parts may amount to as much as 4 or 5 dioptries.

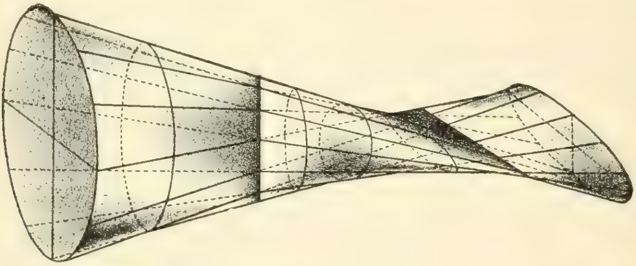

Fig. 309.—Refraction by an Astigmatic Surface.—(*Hansell and Sweet.*)

Chromatic Aberration.— When a beam of light is made to pass through a prism, it is decomposed into the primary colors owing to a difference in the refrangibility of the rays. In passing through the refracting media of the eye the different rays composing white light also undergo unequal refraction and those rays which give rise to one color are brought to a focus at a point somewhat different from those which give rise to other colors. If the eye is accommodated for one set of rays, it is not for another, and the result is a fringe of colors around the image. This defect in the normal eye is so slight that the mind fails to take cognizance of it. That the eye is incapable simultaneously of focalizing rays of widely different refrangiblity, as those which give rise to the blue and red colors, is shown by the following experiment: The eye being directed to a luminous point, a plate of cobalt-glass is placed between the light and the observer close to the eye. This substance has the property of intercepting all rays but the red and the blue and hence these alone will be seen. The center of the image produced will be red and clearly defined, the periphery blue and ill-defined. The reason for this is clear. The eye more readily accommodates itself for the red rays, and hence their focal point is distinct. The blue rays, having a higher degree of refrangibility, come to a focus, cross and diverge, and give rise to diffusion-circles. If a biconcave glass be placed before the cobalt, the blue rays can be focalized on the retina, while the red will fall on the retina without focalization. The image will now be blue and distinct in the center, the periphery red and ill-defined. With the removal of the minus glass the reverse condition again obtains.

Imperfect Centering.—From a purely physical point of view, the eye is not a perfect optic instrument. In addition to the defects noticed in the foregoing paragraphs, there is yet another, viz.: an imperfect centering of the refracting surfaces. In first-class optic instruments the lenses are centered—that is, their optic centers are situated on the same axis. In viewing an object through such a system the visual line corresponds with the axis of the lens system. This is not the case with the refracting system of the eye. A line passing through the center of the cornea and the center of the eye, the *optic axis* (O A in Fig. 310), does not pass exactly through the center of the lens and does not fall into the point for most distinct vision, the fovea. This has lead to the recognition of other lines the relations of which must be kept in mind in all optic discussions, viz.:

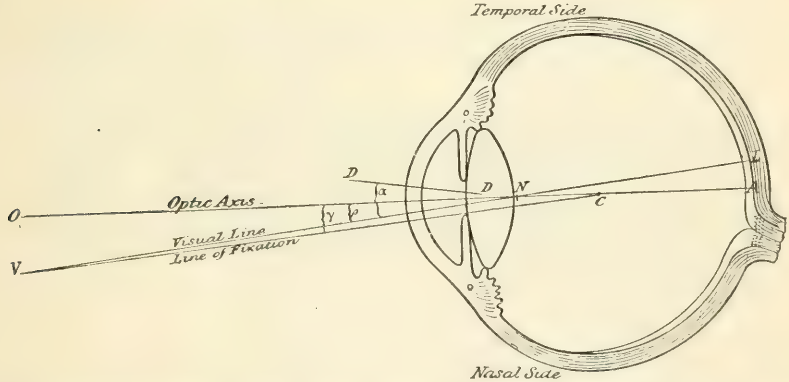

Fig. 310.—Diagram showing the Corneal Axis *D D*, the Optic Axis *O A*, the Visual Axis *V L*, and the Line of Fixation *V C*; also the Three Angles, *α*, *β*, *υ*.

1. The *visual axis* or *visual line* (*V L*), the line connecting the point viewed, the nodal point, and the fovea centralis.
2. The *line of fixation* or *line of regard* (*V C*), the line connecting the point viewed with the center of rotation, the latter being situated 6 mm. behind the nodal point of the eye and 9 mm. before the retina. The relation of these lines and certain angles connected with them are shown in Fig. 327. The angle included between the line *D D* (the major axis of the corneal ellipse) and the visual line is the angle *alpha*, amounting on the average to 5°. The angle incuded between the optic axis and the line of fixation or regard is the angle *gamma*, while the angle between the optic axis and the line of vision is the angle *beta*. In emmetropia the angle *alpha* is about 5°. In hypermetropia it is greater, amounting to 7° or 8°,

giving to the eye an appearance of divergence. In myopia it is much smaller—2°—or in extreme cases may be abolished, the line of vision corresponding with the optic axis or even passing beyond it. The angle *gamma* is of value in determining the actual deviation of the eye in squint.

Functions of the Retina.—Of all the layers of the retina, the rods and cones appear to be the most essential to vision. It is only this layer that is capable of receiving the light stimulus and of transforming it into some specific form of energy, which in turn arouses in the fibers of the optic nerve the characteristic nerve impulses. A ray of light entering the eye passes entirely through the various layers of the retina, and is arrested only upon reaching the pigmentary epithelium in which the rods and cones are embedded. As to the manner in which the objective stimuli—light and color, so called—are transformed into nerve impulses, but little is known. It is probable that the ether vibrations are transformed into heat, which excites the rods and cones. These, acting as highly specialized end-organs of the optic nerve, start the impulses on their way to the brain, where the seeing process takes place. As to the relative function of the rods and cones, it has been suggested, from the study of the facts of comparative anatomy, that the rods are impressed only by differences in the intensity of light, while the cones, in addition, are impressed by qualitative differences in color. The nerve-fibers themselves are insensible to the impact of the ether vibrations, and require for their excitation some intermediate form of energy. That this is the case was shown by Donders, who reflected a beam of light on the optic nerve at its entrance without the individual experiencing any sensation of light. This region, occupied only by the optic-nerve fibers and devoid of any special retinal elements, is therefore an insensitive or *blind spot.* The diameter of this spot is about 1.5 mm., and occupies in the field of vision a space of about 6°. It is situated about 3.5 mm. to the nasal side of the visual axis. Its existence can be demonstrated by the familiar experiment of Mariotte, which consists in placing before the eye two objects having the relation to each other shown in Fig. 311. With the left eye closed and the right eye directed to the cross, both objects may be visible. But by moving the figure away from or toward the eye, there will be found a distance, about 30 cm., when the circle will be invisible. This occurs when the image falls on the optic nerve at its entrance. The experiment of Purkinje as described in the following paragraph demonstrates also the fact that the sensitive portion of the retina is to be found only in the layer of rods and cones.

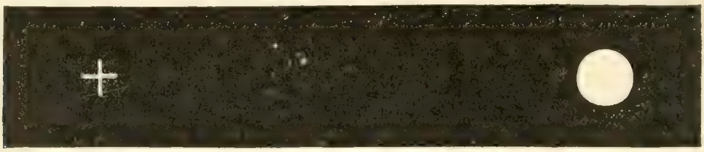

Fig. 311.—Diagram for Observing the Situation of the Blind Spot.—(*Helmholtz.*)

It is well known that the blood-vessels of the retina are situated in its innermost layers a short distance behind the optic nerve-fibers. Owing to this anatomic arrangement, a portion of the light coming through the pupil will be intercepted by the vessels and a shadow projected on the layer of rods and cones. Ordinarily, these shadows are not perceived, for the reason that the shaded parts are more sensitive, so that the small amount of light passing through the vessels produces as strong an impression on this part as does the full amount of light on the unshaded parts of the retina, and perhaps because the mind has learned to disregard them. But if light be made to enter the eye obliquely, the position of the shadows will be changed, when at once they become apparent. This can be shown in the following way: If in a darkened room a lighted candle be held several inches to the side and to the front of the eye, and then moved up and down, there will be perceived, apparently in the field of vision, an arborescent figure corresponding to the retinal blood-vessels. This is due to the falling of the shadows on unusual portions of the layer of rods and cones.

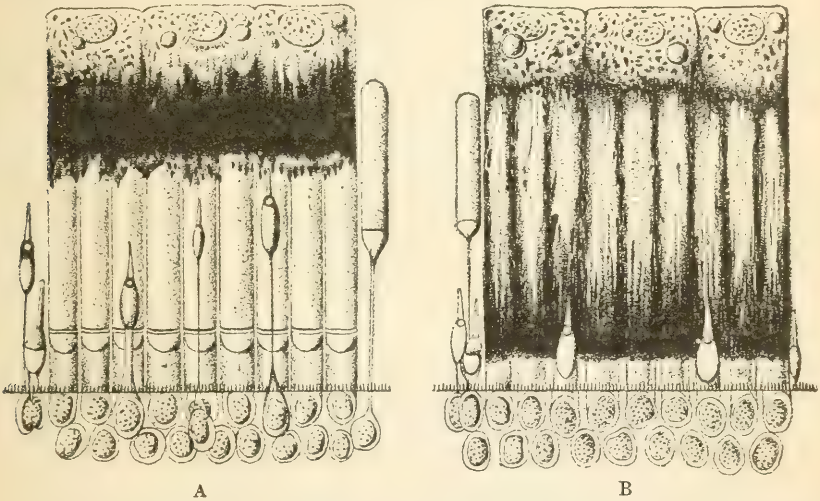

FIG. 312.—SECTION OF THE RETINA OF A FROG. A. In darkness. B. In light.—(*After Van Genderen Stort, from Tscherning's "Physiologic Optics."*)

Excitability of the Retina.—The retina is not equally excitable in all parts of its extent. The maximum degree of sensibility is found in the macula lutea, and especially in its central portion, the fovea. In this region the layers of the retina almost entirely disappear, the layers of rods and cones alone remaining, and in the fovea only the cones are present. That this area is the *point of most distinct vision* is shown by the observation that when the eye is directed to any given point of light, its image always falls in the fovea. Any pathologic change in the fovea is attended by marked indistinctness of vision. The sensibility of the retina gradually but irregularly diminishes from the macula toward the periphery. This diminution in insensibility holds true for monochromatic as well as white light.

As stated above, the nature of the molecular processes which take place in the retinal tissue, caused on one hand by the light vibrations, and on the other hand developing nerve impulses, is entirely unknown. The discovery of the *visual purple* in the outer segment of the rods gave promise of some explanation of the process, especially when it was shown to undergo changes when exposed to the action of light. But as the pigment is wanting in the cones, and especially in the fovea, it cannot be considered essential to distinct vision, although that it plays some important rôle in the visual process is highly probable. It was observed by Van Genderen Stort, that when an animal is kept in darkness some time before death, the cones are long and filiform; but if the animal has been exposed to light, they are short and swollen. It was discovered by Boll that if an animal is kept in darkness an hour or two before death the pigment is massed at the ends of the rods and cones, but after exposure to light it becomes displaced and extends over and between the rods almost to the external limiting membrane. These conditions are represented in Fig. 312.

The Eye a Living Camera.—In its construction, in the arrangement of its various parts, and in their mode of action the eye may be compared to a *camera obscura.* Though the comparison may not be absolutely exact, yet in a general way it is true that there are many striking points of similarity between them; *e.g.*, the sclera and chorioid may be compared to the walls of the camera; the combined refracting media to the component glasses of the lens, the action of which results in the focusing of the light rays; the retina to the sensitive plate receiving the image formed at the focal point; the iris to the diaphragm for the regulation of the amount of light to be admitted, and for the partial exclusion of those marginal rays which give rise to *spheric aberration;* the ciliary muscle to the adjusting screw, by means of which the image is brought to a focus on the sensitive plate, notwithstanding the varying distances of the object from the lens. The presence of the *visual purple* in the rods of the retina capable of being altered by light makes the comparison still more striking.

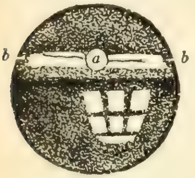

FIG. 313.—RETINA OF A RABBIT. OPTOGRAM OF A WINDOW FOUR METERS DISTANT *a.* Yellow spot. *b, b.* Streak of Medullated nerve-fibers.—(*Kühne.*)

Kühne even succeeded in obtaining a fixed image or an *optogram* of an external object in a manner similar to that by which an image is fixed on the sensitive plate of a camera. An animal is kept in the dark for about ten minutes in order to permit the retinal pigment to be completely regenerated. The animal, with the eyes covered, is then brought into a room with a single window. While the head is steadily directed to the window, the eye is exposed for several minutes. The eyes are again covered, the animal killed, and the eyes removed by the light of a sodium flame. The retina is then placed in a 4 per cent. solution of alum. In a short time the image of the window, the *optogram*, will be fixed (Fig. 313). That portion of the image corresponding to the window lights will be quite bleached in appearance from the action of the light on the pigment, while that corresponding to window bars will have the usual color of the retina. During life the regeneration of the visual purple must take place with extreme rapidity if a similar change takes place with the formation of each image. The visual purple is believed to be derived from a pigment secreted by the layer of pigment cells.

Binocular Vision.—Though two images are formed, one on each retina, when the eyes are directed to a given object, there results but one sensation. If the direction of either visual axis be changed by pressure on the eyeball, there arise two sensations, and the object appears to be doubled. The reason assigned for this, in the first instance, is that the two images fall into the foveæ, on two corresponding points; while in the second instance they fall on non-corresponding points. It would appear, therefore, that for the purpose of seeing an object singly when the eyes are directed toward it, the rays emanating from it must fall on corresponding parts of the retina. As all portions of the retina are sensitive to light, though in varying degrees, it is not essential that the images always fall in the foveæ. The parts of the retinæ which correspond physiologically are shown in Fig. 314. In this figure the retinal area is divided into quadrants by vertical and horizontal lines of separation, as they are termed. If one retina is placed in front of or over the other, it will be found that the quadrants bearing similar letters cover each other. So long as the rays of light, entering the eye, fall on corresponding areas the sensation of but one object arises. If, however, they fall on non-corresponding areas, two sensations arise. Normal binocular vision enlarges very considerably the area of the visual field, permits of a better estimation of the size and distance of objects, enables the mind to form more readily a perception of depth, and increases the intensity of sensations.

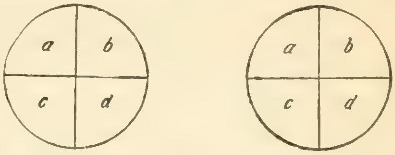

FIG. 314.—CORRESPONDING AREAS OF THE RETINA.

The Horopter.—When the eyes are in a so-called secondary position —that is, in a position in which the visual axes are converged and directed to a point in front of and in the middle plane of the body—it will be found on examination that rays of light from a number of other objects enter the eye, pass through the nodal point, and fall on corresponding parts of the two retinæ and give rise to but single images. All such points lie, for the horizontal line of separation, on a line termed the *horopter*. The form of this line is that of a circle which passes through the fixation point and the two nodal points. Any object on the horopter will give rise to but a single image. This is shown in Fig. 315, in which the objects I, II, III project their rays into both eyes and upon corresponding areas.

In addition to the horopter for the horizontal line of separation, there is also an horopter for the vertical line of separation. At a distance of two meters the vertical horopter is a plane. Within this distance it is concave to the face; beyond this distance it is convex.

An object which lies either in front of or behind the fixation point will project its rays on parts of the retinæ which do not correspond, and hence give rise to double images. This is evident from examination of Fig. 316. While the eyes are directed to figure 2, of which there is but a single image, the objects B and A give rise to double images, for reasons already given. If the eyes are now directed to B, double images will be formed of 2 and A.

At all times, therefore, double images are formed on the retinæ the existence of which is scarcely noticed unless the attention is directed to them. This is due to the fact that many of the images fall on the peripheral, less sensitive parts of the retinæ. At the same time, from a want of accommodation and the formation of diffusion-circles, they are indistinct. For these reasons they are readily neglected.

In the primary position of the eyes—that is, a position in which the visual axes are parallel—the horopter is a plane at infinity. In the tertiary positions the horopter is a curve of complex form.

Movements of the Eyeball.—The almost spheric eyeball lies in the correspondingly shaped cavity of the orbit, like a ball placed in a socket, and is capable of being rotated to a considerable extent by the six muscles which are attached to it. These muscles are the superior and inferior recti, the external and internal recti, and the superior and inferior obliqui. The four *recti* muscles arise from the apex of the orbit cavity, from which point they pass forward to be inserted into the sclera about 7 to 8 mm. from the corneal border. The *superior oblique* muscle having a similar origin passes forward to the upper and inner angle of the orbit cavity, at which point its tendon passes through a cartilaginous pulley, after which it is reflected backward to be inserted into the superior surface of the sclera about 16 mm. behind the corneal border. The *inferior oblique* muscle arises from the inner and inferior angle of the orbit cavity. It then passes outward, upward, and backward, to be inserted into the upper, posterior, and temporal portion of the sclera about 4 or 5 mm. from the optic nerve entrance.

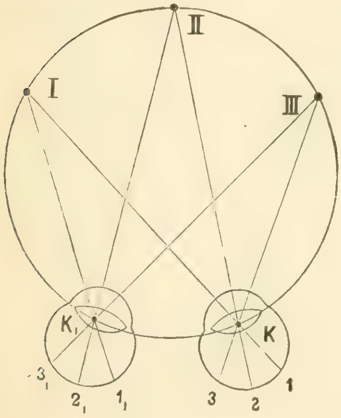

Fig. 315.—Horopter for the Secondary Position, with Convergence of the Visual Axes. —(*Landois.*)

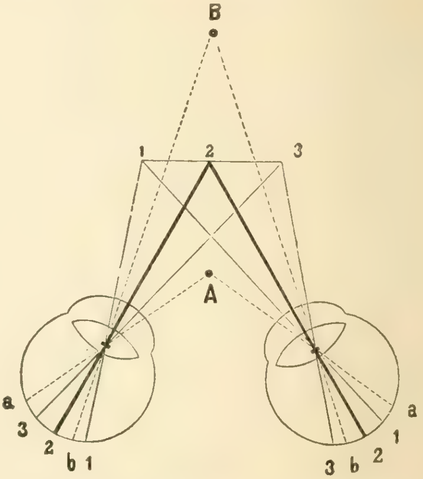

Fig. 316.—Scheme of Identical and Non-identical Points of the Retina.—(*Landois.*)

The movements of each eye are referred to three fixed lines or axes, which have their origin at the point of rotation of the eyeball, this point lying about 1.7 mm. behind the center of the globe. If the eye looks straight forward in the horizontal plane (the head being erect), the line joining the center of rotation with the object looked at is the *line of fixation* or *line of regard*. Around this antero-posterior axis the eye may be regarded as performing its circular *rotation* or *torsion*. At right angles to this line, and joining the centers of rotation of both eyes, is the *horizontal* or *transverse* *axis*, around which the movements of elevation (up to 34 degrees) and depression (down to 57 degrees) take place. At right angles to both of these lines there is the *vertical axis*, around which the movements of adduction (toward the nose up to 45 degrees) and abduction (toward the temple up to 42 degrees) occur. The six muscles may be divided into three pairs, each of which has a common axis around which it tends to move the eyeball. But only the common axis of the internal and external recti coincides with one of three axes before mentioned—namely, with the vertical axis—thus moving the ball only inwardly or outwardly—respectively. The other two pairs, however, have their own axes of action, and their movements of the ball must be, therefore, analyzed with regard to all the three axes, each of these four muscles producing rotation, elevation, and depression, and abduction or adduction. The superior and inferior recti muscles, forming one pair, move the eye around a horizontal axis which intersects the median plane of the body in front of the eyes at an angle of 63 degrees, and the superior and inferior oblique muscles forming the third pair rotate the globe around a horizontal axis which cuts the median plane of the body behind the eyes at an angle of 39 degrees. Thus it is that each muscle moves the eye as follows, the movement for practical purposes being referred to the cornea: The rectus externus draws the cornea simply to the temporal side, the rectus internus simply to the nose; the superior rectus displaces the cornea upward, slightly inward, and turns the upper part toward the nose (medial torsion); the inferior rectus moves the cornea downward, slightly inward, and twists the upper part away from the nose (lateral torsion); the superior oblique displaces the cornea downward, slightly outward, and produces medial torsion; while the inferior oblique moves the cornea upward, slightly outward, and produces lateral torsion. These facts show that for certain movements of the eye at least three muscles are necessary (see following table):

Inward	Rectus internus.	*Inward and downward*	Rectus internus. Rectus inferior. Obliquus superior.
Outward	Rectus externus.	*Outward and upward*	Rectus externus. Rectus superior. Obliquus inferior.
Upward	Rectus superior. Obliquus inferior.	*Outward and downward*	Rectus externus. Rectus inferior. Obliquus superior.
Downward	Rectus inferior. Obliquus superior.		
Inward and upward	Rectus internus. Rectus superior. Obliquus inferior.		

If both eyes have their line of vision in the horizontal plane parallel with each other and with the median plane of the body, they are said to be in the *primary position*. All other positions are called *secondary* and *tertiary*. Both eyes always move simultaneously, which is called the *associated movement of the eyes*. There are three forms of associated movements: (1) movement of both eyes in the same direction; (2) movements of convergence by which the visual lines are converged on a point in the middle line of the body; (3) movements of divergence, by which the eyes are brought back from convergence to parallelism, or even to divergence, as in certain stereoscopic exercises. A combination of (1) and (2) or of (1) and (3) takes place for certain positions of the object looked at.

Color-perception.—A beam of sunlight passed through a glass prism is decomposed into a series of colors—red, orange, yellow, green, blue, and violet—the so-called *spectral colors*, so well exemplified in the rainbow. The spectral colors are termed *simple colors*, because they cannot be any further decomposed by a prism. Objectively, the spectral colors consist of very rapid transverse electro-magnetic vibrations of the ether, from about 400 millions of millions per second for red to about 760 millions of millions for violet, but subjectively they are sensations caused by the impact of the ether-waves on the percipient layer of the retina.

It is possible to mix or blend these spectral color-sensations in the eye by stimulating the same area of the retina by different spectral colors, either at the same time or in rapid succession. The following table shows the results of such experiments as performed by v. Helmholtz (Dk. =dark; Wh. =whitish):

	Violet	Indigo	Cyan-blue	Bluish-green	Green	Greenish-yellow	Yellow
Red.	Purple.	Dk.-rose.	Wh.-rose.	White.	Wh.-yellow.	Gold-yellow.	Orange.
Orange.	Dk.-rose.	Wh.-rose.	White.	Wh.-yellow.	Yellow.	Yellow.	....
Yellow.	Wh.-rose.	White.	Wh.-green	Wh.-yellow.	Gr.-yellow.	....	......
Gr.-yellow.	White.	Wh.-green.	Wh.-green.	Green.	....	....	......
Green.	White-blue.	Water-blue.	Bl.-green.	....	....	....	......
Bluish-green.	Water-blue.	Water-blue.	....	....	....	....	......
Cyan-blue.	Indigo.	....	....	....	....	....	......

These are the *mixed colors*. But it is to be observed that only two new color-sensations can be produced, white and purple, the remaining mixed colors already finding their equivalent in the spectrum. White and purple, therefore, are color-sensations which have no objective equivalent in a simple number of ether-vibrations like the spectral colors.

Two spectral colors which by their mixture produce the sensation of white are called *complementary colors*. Such are red and green-blue, golden yellow and blue, green and violet. The mixture of all the spectral colors produces white again. This is the result of adding two or more *color-sensations*. Different results are obtained, however, by adding color *pigments*. Yellow and blue, for example, produce in the eye white, but on the painter's palette green. The colors of nature are usually mixtures of simple colors, as can be shown by spectroscopic analysis or by a synthesis of spectral colors.

In all color-sensations we must distinguish three primary qualities: (1) hue; (2) purity or tint; (3) brightness or luminosity. The first quality gives the main name to the color—*e.g.*, red or blue—this depending on the spectral color or the mixture of two spectral colors with which it can be matched. The second quality, the tint, depends on the admixture of white with the ground color; and the third quality, brightness, depends on the objective intensity of the light and the subjective sensitiveness of the retina. Color-perception thus far refers only to the most sensitive part of the retina. At the more peripheral parts of the retina the colors are seen somewhat differently, as is shown by the following table giving the limits up to which the colors are recognized:

	White.	Blue.	Red.	Green.
Externally	90°	80°	65°	50°
Internally	60°	55°	50°	40°
Superiorly	45°	40°	35°	30°
Inferiorly	70°	60°	45°	35°

Theories of Color-perception.—*The theory of v. Helmholtz*, originated by Thomas Young (1807), assumes in its latest form the existence in the human retina of three different kinds of end-organs, each of which is loaded with its own photo-chemical substance capable of being decomposed by a certain color, and thus exciting the fiber of the optic nerve.

In the first group these end-organs are loaded with a red-sensitive substance, which is affected mainly by the red part of the spectrum; the second group has its end-organs provided with a green-sensitive substance, which is mainly excited by the green color; while the third group is provided with a blue-sensitive substance, this latter being mainly affected and decomposed by the blue-violet portion of the spectrum. All these three different end-organs are present in every part of the most sensitive area of the retina, and are connected by separate nerve-fibers with special parts of the brain, in the cells of which each calls up its separate sensation of red or green or blue.

Out of these three primary color-sensations all other color-sensations arise. If a light mainly excites the red- or green- or blue-sensitive substance of a retinal area, we term it red, green, or blue, respectively. But if two of these photo-chemical substances are stimulated simultaneously, quite different sensations arise. Thus simultaneous stimulation of the red and green substances gives rise to the sensation of yellow, that of red and blue to the sensation of purple, and that of blue and green to the sensation of blue-green. Simultaneous stimulation of all three substances of a certain area produces the sensation of white. According to this theory, complementary colors are any two which together excite all three substances. *Color-blindness* is explained by this theory, on the assumption that two of the photo-chemical substances have become similar or equal in composition to each other.

The *theory of Hering*, brought forward in 1874, has the underlying assumption that the process of restitution in a nerve-element is capable of exciting a sensation. This theory asserts that there are three visual substances in the retina—a white-black, a red-green, and a yellow-blue visual substance. A destructive process in the white-black substance, such as is induced not only by white light, but also by any other simple or mixed color, produces the sensation of white, while the process of restitution or assimilation in this substance produces the sensation of black. Similarly, red light produces dissimilation or decomposition in the red-green substance, and this, again, the sensation of red. Green light, however, favors the process of restitution or assimilation in the red-green substances, and thus gives rise to the sensation of green. In the same way the sensation of yellow has its cause in the decomposition of yellow-blue substance induced by yellow light, while the sensation of blue is produced by an assimilative process in the same substance. Simultaneous processes of dissimilation and assimilation in the same visual substance antagonize each other, and consequently produce no color-sensation by means of this substance, but only the sensation of white, by reason of decomposition, by both colors, in the white-black substance. Thus, yellow and blue, impinging on the same retinal area, have no effect on the yellow-blue substance, because they are antagonistic in their action on this substance, but produce only the sensation of white, as both yellow and blue decompose the white-black material. *Color-blindness* is explained by the assumption of the absence of either the red-green or the yellow-blue visual substance in the retina.

Accessory Structures.—The eyeball is protected anteriorly by the eyelids and their associated structures, the Meibomian glands, the lachrymal glands, and tears.

The *eyelids* consist of a central framework of connective tissue supporting muscle-tissue (the orbicularis palpebrarum muscle) and glands, and covered externally by skin and internally by a modified skin, the conjunctiva. The free border of each lid is strengthened by a semilunar plate of dense fibrous tissue, the tarsus. The cutaneous edge of the lid is bordered with short stiff hairs. At the inner extremity each eyelid presents a small opening, the *punctum lacrimale*, the beginning of the lachrymal duct. The two ducts after uniting open into the nasal duct.

The *Meibomian glands* are modified sebaceous glands imbedded in the posterior portion of the lids. Their ducts open on the free border of the lid. These glands secrete an oleaginous material resembling sebaceous matter, which accumulates along the margin of the lid and prevents the tears from flowing down the cheek.

The *lachrymal gland* is situated at the upper and outer part of the orbit cavity. It consists of a series of compound tubules lined by epithelium. The secretion (the tears) is conducted from the gland to the outer part of the conjunctiva by seven or eight ducts. The lachrymal secretion consists of water and inorganic salts. It is distributed over the corneal surface during the act of winking, thus keeping it moist and free from foreign particles. It eventually passes into the lachrymal ducts and then into the nose. The lachrymal glands receive secretory fibers by way of the fifth nerve and the cervical sympathetic. The secretion can be excited reflexly from stimulation of sensor nerves as well as by emotional states.

CHAPTER XXX

THE SENSE OF HEARING

The physiologic mechanism involved in the sense of hearing includes the ear, the acoustic nerve, the acoustic tract (the lateral fillet or lemniscus), the acoustic radiation, and nerve-cells in the cortex of the temporal lobe.

Peripheral stimulation of this mechanism develops nerve impulses which, transmitted to the cerebral cortex, evoke the sensation of sound and its varying qualities—intensity, pitch, and timbre.

The specific physiologic stimulus to the terminal organ, the organ of Corti, is the impact of atmospheric pulsations of varying energy and rapidity.

THE PHYSIOLOGIC ANATOMY OF THE EAR

The ear, the organ of hearing, is lodged within the petrous portion of the temporal bone. It may, for convenience of description, be divided into three portions: viz., the external, the middle, and the internal portion (Fig. 317).

The External Ear.—The external ear consists of the *pinna* or *auricle* and the *external auditory canal.*

The Pinna.—The pinna is composed of a thin layer of cartilage which presents a series of elevations and depressions. It is attached by fibrous tissue to the outer edge of the auditory canal and covered by a layer of skin continuous with that covering adjacent structures. The general shape of the pinna is concave. Its anterior surface presents, a little below the center, a deep depression—the *concha.*

The External Auditory Canal.—The external auditory canal extends from the concha inward for a distance of from 25 to 30 mm. It is directed at first upward, forward, inward, and then somewhat downward to its termination. It is composed partly of bone and partly of cartilage and lined by a reflection of the skin covering the pinna. At the external portion of the canal the skin contains a number of tubular glands, the *ceruminous glands*, which resemble in their conformation the perspiratory glands. They secrete cerumen or earwax.

The Middle Ear.—The middle ear, or tympanum, is an irregularly shaped cavity hollowed out of the temporal bone and situated between the external auditory canal and the internal ear. It is narrow from side to side, though wider above than below. It is relatively long in its antero-posterior and vertical diameters. The upper portion is known as the attic. The middle ear is in communication posteriorly with the mastoid cells, anteriorly with the pharynx through the Eustachian tube.

The *Eustachian Tube.*—The passageway between the tympanic cavity and the naso-pharynx is known from its discoverer as the Eustachian tube. It is composed internally of bone, externally of cartilage, and is lined by mucous membrane covered with ciliated epithelium. Near the middle of its course the tube is contracted, though expanded at either extremity (Fig. 317). It measures about 40 mm. in length. Its general direction from the pharyngeal orifice is outward, backward, and upward at an angle of about 45 degrees.

The middle ear cavity is separated from the external ear by a membrane —the membrana tympani—and from the internal ear by an osseo-membranous partition which forms a common wall for both cavities. The interior of the cavity is crossed from side to side by a chain of bones and lined by a mucous membrane continuous with that lining the pharynx.

The Membrani Tympani.—The membrana tympani, is a thin, translucent nearly circular membrane, measuring about 10 mm. in diameter, placed at the inner termination of the external auditory canal. It is inclosed in a ring of bone which in the fetal condition can be easily removed, but in the adult condition cannot be removed, owing to its consolidation with the surrounding bone. This membrane consists primarily of a layer of fibrous tissue which is covered externally by a thin layer of skin continuous with that lining the auditory canal, and internally by a thin mucous membrane. The tympanic membrane is placed obliquely at the bottom of the auditory canal, inclining from above and behind downward and forward at an angle of about forty-five degrees. The external surface of this membrane presents a funnel-shaped depression, the sides of which are slightly convex.

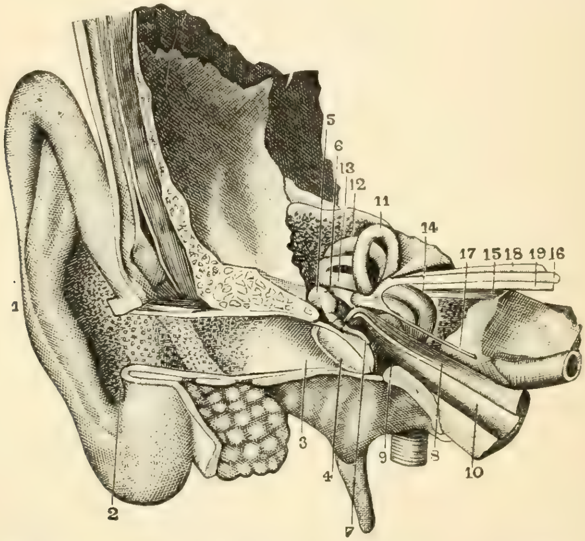

FIG. 317.—THE EAR. 1. Pinna, or auricle. 2. Concha. 3. External auditory canal. 4. Membrana tympani. 5. Incus. 6. Malleus. 7. Manubrium mallei. 8. Tensor tympani. 9. Tympanic cavity. 10. Eustachian tube. 11. Superior semicircular canal. 12. Posterior semicircular canal. 13. External semicircular canal. 14. Cochlea. 15. Internal auditory canal. 16. Facial nerve. 17. Large petrosal nerve. 18. Vestibular branch of auditory nerve. 19. Cochlear branch.—(*Sappey.*)

The Ear-bones.—Running across the tympanic cavity and forming an irregular line of joined levers is a chain of bones, which articulate one with another at their extremities. These bones are known as the *malleus*, *incus*, and *stapes*. The form and arrangement of these bones are shown in Figs. 318, 319.

The *malleus*, or hammer bone, consists of a head, neck, and handle, of which the latter is attached to the inner surface of the membrana tympani. The *incus* or anvil bone presents a concave articular surface which receives the head of the malleus. The *stapes*, or stirrup bone, articulates externally with the long process of the incus, and internally, by its oval base, with the edges of an oval opening, the foramen ovale. The entire chain is partially supported by a ligament attached to the shrot process of the incus and to the walls of the tympanic cavity.

The Tensor Tympani Muscle.—This is a delicate muscle, about 15 mm. in length, situated in a narrow groove just above the Eustachian tube (Fig. 320). It arises from the cartilaginous portion of the Eustachian tube and the adjacent portion of the sphenoid bone. From this origin it passes nearly horizontally backward to the tympanic cavity; just opposite the foramen ovale its tendon bends at a right angle over the processus cochleariformis and then passes outward across the tympanic cavity to be inserted into the handle of the malleus near the neck.

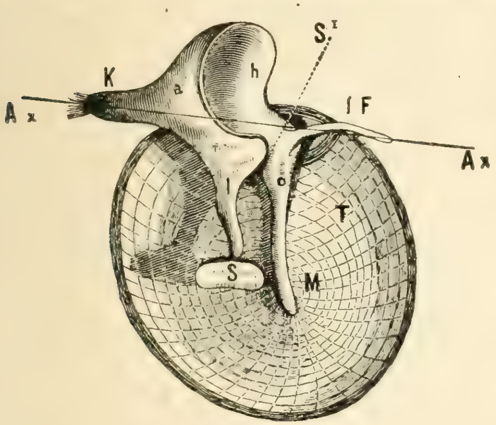

Fig. 318.—Tympanic Membrane and the Auditory Ossicles (Left) seen from within, *ie.*, from the Tympanic Cavity. *M*. Manubrium or handle of the malleus. *T*. Insertion of the tensor tympani. *h*. Head. *lF*. Long process of the malleus. *a*. Incus, with the short (*K*) and the long (*l*) process. *S*. Plate of the stapes. *Ax*, *Ax*, is the common axis of rotation of the auditory ossicles. S^1. The pinion-wheel arrangement between the malleus and incus.—(*Landois.*)

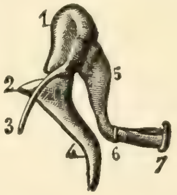

Fig. 319.—Auditory Ossicles. 1. Head of malleus. 2. Processus brevis. 3. Processus gracilis. 4. Manubrium. 5. Long process of incus. 6. Articulation between incus and stapes. 7. Stapes. —(*Sappey.*)

The Stapedius Muscle.—The stapedius muscle emerges from the cavity of a pyramid of bone which projects from the posterior wall of the tympanum. Its tendon passes forward to be inserted into the neck of the stapes bone near its point of articulation with the incus.

The Internal Ear.—The internal ear, or labyrinth, is located within the petrous portion of the temporal bone. It consists of an osseous and a membranous portion of which the latter is contained within the former.

The **osseous labyrinth** is subdivided into vestibule, semicircular canals, and cochlea.

The Vestibule.—The vestibule is a small, triangular-shaped cavity between the semicircular canals and the cochlea. It is separated from the cavity of the middle ear by an osseous partition which presents near its center an oval opening, the *foramen ovale.* (See Fig. 322.) In the living condition this opening is closed by the base of the stapes bone, which is held in position by an annular ligament. The inner wall presents a number of openings for the passage of nerve-fibers.

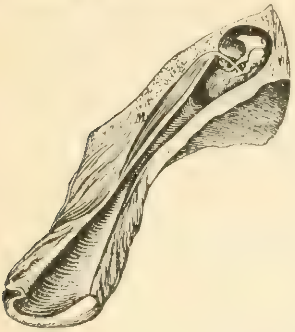

FIG. 320.—M, THE TENSOR TYMPANI MUSCLE—THE EUSTACHIAN TUBE (LEFT).—(*Landois.*)

The Semicircular Canals.—The semicircular *canals* are three in number, and named from their position, the superior vertical, the posterior vertical and the horizontal. These canals are at right angles one to the other and open by five orifices into the vestibule, one of the orifices, however, being common to two of the canals. Each canal near the vestibular orifice is enlarged to almost twice the size of the rest of the canal forming what has been termed the ampulla. The superior canal is placed transversely to the long axis of petrous portion of the temporal bone; the posterior canal is placed almost parallel to the posterior surface of the petrous portion of the temporal bone. The lateral or horizontal canal is placed horizontally to the vertical canals. Their relation to one another on opposite sides of the median plane of the body is shown in Fig. 321. From the anatomic relations of these canals, it is apparent that the horizontal or lateral canals lie in one and the same plane; that the two superior vertical canals, as well as the two posterior vertical canals, lie in planes which are at right angles to each other, and that the superior vertical canal of the one side, lies in a plane parallel to the plane in which the posterior vertical canal of the opposite side lies.

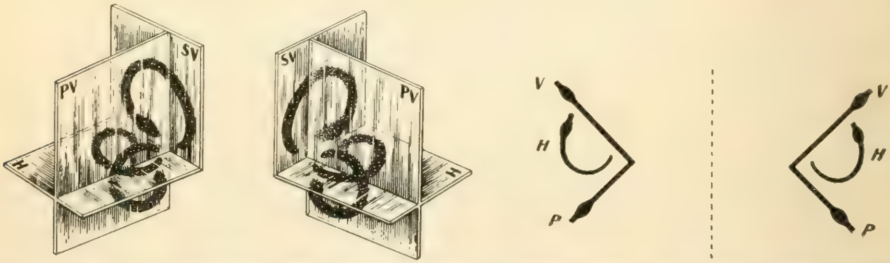

FIG. 321.—DIAGRAMS OF SEMICIRCULAR CANALS TO SHOW THEIR POSITION IN THREE PLANES AT RIGHT ANGLES TO ONE ANOTHER. It will be seen that the two horizontal canals lie in the same plane(H), and that the superior vertical of one side (SV) is in the same plane as the posterior vertical (PV) of the other side.—(*from Ewald.*)

The Cochlea.—The cochlea, the anterior portion of the labyrinth, is a gradually tapering canal, about 35 mm. in length, wound spirally two and a half times around a central bony axis, the *modiolus.* The cavity of the cochlea is partially subdivided into two cavities by a thin spiral plate of bone which projects from the inner wall, known as the *lamina ossea spiralis.* In the natural condition this partition is completed by a connective-tissue membrane, so that the two passages are completely separated from each other.

The *upper* passage or scala is in free communication with the vestibule, and is known as the *scala vestibuli;* the *lower* passage or scala in the dead condition communicates with the tympanum by means of a round opening, the *foramen rotundum,* and is, therefore, known as the *scala tympani.* In the living condition this opening is completely closed by a membrane, a second membrana tympani. Both the scalæ vestibuli and tympani communicate at the apex of the cochlea by a small opening, the helicotrema. The modiolus, the central bony axis, is perforated from base to apex by a canal for the passage of the auditory nerve-fibers; lateral canals, diverging from the central canal, pass through the osseous lamina spiralis and transmit fibers of the auditory nerve. The interior of the bony labyrinth is lined by periosteum covered by epithelium and in communication with lymph-spaces at the base of the skull by means of the aqueduct of the vestibule.

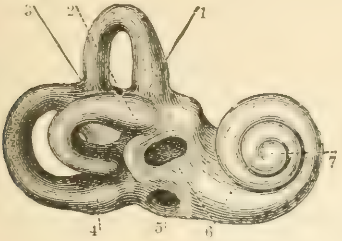

FIG. 322.—BONY COCHLEA. 1. Ampulla of superior semicircular canal. 2. Horizontal canal. 3. Junction of superior and posterior semicircular canals. 4. The posterior semicircular canal. 5. Foramen rotundum. 6. Foramen ovale. 7. Cochlea.

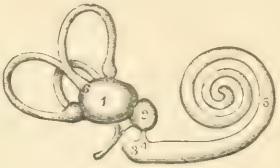

FIG. 323.—1. Utricle. 2. Saccule. 3. Vestibular end of cochlea. 4. Canalis reuniens. 5. Membranous cochlea. 6. Membranous semicircular canals.

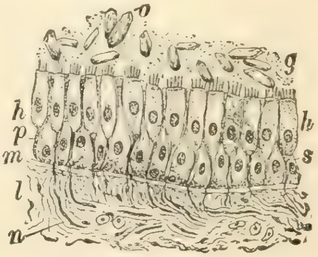

FIG. 324.—SECTION OF WALL OF UTRICLE OF THE INTERNAL EAR, through macular region, from rabbit, showing otoliths (*o*), embedded within granular substance (*g*). *h.* Ciliated cells with processes. (*p*), extending between sustentacular elements (*s*). *m.* Basement membrane. *n.* Nerve-fibers within fibrous tissue (*l*) passing toward hair-cells and becoming non-medullated at basement-membrane.—(*After Piersol.*)

The **membranous labyrinth,** lying within the osseous labyrinth, corresponds with it in form, though it is smaller in size. It may be subdivided into vestibule, semicircular canals, and cochlea (Fig. 323).

The Vestibular Portion.—The vestibular portion consists of two small sacs, the *utricle* and the *saccule,* which communicate with each other by means of the two branches of a duct passing through the aqueduct of the vestibule—the *ductus endolymphaticus.*

The Semicircular Canals.—The semicircular canals, three in number, communicate with the utricle in the same manner as the bony canals communicate with the vestibule. The saccule communicates with the membranous cochlea by a short canal, the *canalis reuniens.* The walls of the utricle, saccule, and semicircular canals are composed of connective tissue lined by epithelium. At the points of entrance of the auditory nerve, the *maculæ acusticæ,* in all three structures, the epithelium undergoes a marked change in appearance and structure. It becomes columnar in shape and provided with stiff hair-like processes or threads, which project into the cavity. In the saccule and utricle the hair-like processes are covered by a layer of small crystals of calcium carbonate held together by a gelatinous material. The crystals are known as otoliths (Fig. 324).

The Vestibular Nerve.—The fibers of the vestibular nerve, arising from the cells of the ganglion of Scarpa in the internal auditory meatus, send their peripherally directed branches through the foramina in the inner wall of the vestibule, through the walls of the utricle and semicircular canals near the ampulla. As the fibers approach the maculæ acusticæ they subdivide into delicate fibrillæ, which ultimately become histologically and physiologically related to the neuroepithelium. From the relation of the nerve-fibers to the epithelium, the latter must be regarded as the highly specialized *terminal organ* of the *vestibular portion* of the auditory nerve.

The Cochlea.—The cochlea is a closed membranous tube situated between the osseous lamina spiralis and the outer bony wall. A transverse section of the entire cochlea shows the relation of the osseous and membranous portions (Fig. 325). The cochlear tube is triangular in shape. The base is attached to the bony wall, the apex to the edge of osseous lamina spiralis. One side of the tube forms in part the membrane of Reissner, the other side forms in part the basilar membrane. The sides of the cochlea toward the scala vestibuli and scala tympani are covered with epithelium. The triangular cavity of the cochlear tube is known as the *scala media*. The *inner surface* of the cochlear tube is lined by epithelium, which becomes extraordinarily modified and specialized along the surface of the basilar membrane, to constitute what is known as

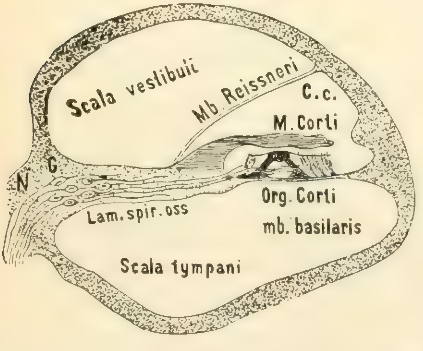

Fig. 325.—A Transverse Section of a Turn of the Cochlea.

The Organ of Corti.—In Fig. 325 this organ is represented as it appears on cross-section of the cochlea. It consists primarily of an arch composed of two modified epithelial cells known as the rods or pillars of Corti, which rest below on the basilar membrane, but meet and interlock above; it consists secondarily of a series of columnar epithelial cells provided with hair-like processes which rest upon and are supported by the rods both on the inner and outer aspects of the arch. The space beneath the arch is known as the tunnel. The inner hair cells are not nearly so numerous as the outer hair cells. The epithelial cells external to the outer and inner hair cells are supporting or sustentacular in character.

The organ of Corti extends the entire length of the cochlea. The number of rods which, standing side by side, form the inner limb of the arch is estimated at 5600; the number which form the outer limb is estimated at 3850. The outer rods are broader than the inner and at some places articulate with two or three inner rods. The upper edges of the rods are flattened, elongated, and project outward, forming a reticulated membrane through the meshes of which the hair-like processes of the cells project.

From the connective-tissue thickening on the upper surface of the osseous lamina spiralis there extends outward over the organ of Corti a thin membrane, the *membrana tectoria.* The common cavity between the walls of the osseous and membranous labyrinth in the vestibule, the semicircular canals, in the scala vestibuli and scala tympani of the cochlea, is filled with a clear fluid—the *perilymph;* the common cavity within the walls of the entire membranous labyrinth is also filled with a similar fluid—the *endolymph.* The hair-like processes of the epithelial cells covering the maculæ acusticæ and the rods of Corti are consequently bathed by endolymph. Both fluids are in relation with the subarachnoid lymph-spaces at the base of the brain, the perilymph through the aqueduct of the vestibule, the endolymph through the endolymphatic duct.

The Cochlear Nerve.—The fibers of the cochlear nerve, arising from the ganglion cells of the *spiral ganglion* situated in the osseous lamina spiralis near the modiolus, send their peripheral branches to the saccule and to the organ of Corti. As they approach this structure they lose their medullary sheath and become naked axis-cylinders. The fibers then divide into two parts, of which one passes to the inner hair cells; the other passes between the inner rods and crosses the tunnel between the outer rods to the outer hair cells. The exact method of termination of these fibers in the hair cells is unknown.

From the relation of the nerve-fibers to the organ of Corti the latter must be regarded as the highly specialized *terminal organ* of the cochlear division of the auditory nerve.

THE PHYSIOLOGY OF HEARING

The general function of the ear is the reception of atmospheric vibrations and the transmission of the effects they produce to the percipient elements—the hair cells—of the organ of Corti. The vibratory excitation of these end-organs thus caused, is the basis of auditory perceptions. The atmospheric vibrations are collected by the pinna and concha, conveyed by the auditory canal to the tympanic membrane, transmitted by the chain of bones to the labyrinth to pass successively through the perilymph, the membranous walls, and the endolymph, to the hair cells. The nerve impulses generated by these vibrations are then transmitted by the cochlear (acoustic) nerve to the acoustic centers of the cerebrum, where the sensations of sound are evoked. In this general process each one of the individual structures composing the ear in its entirety, has a special function. In order to fully appreciate these functions the characteristic features of atmospheric vibrations, viz.: intensity pitch and quality must be kept in mind.

Atmospheric Vibrations.—The vibrations of the atmosphere, the objective causes of the sensations of sound, are imparted to the atmosphere by, the vibrations of elastic bodies such as tuning-forks, rods, strings, membranes, etc. These produce in the air a to-and-fro movement of its particles, resulting in a succession of alternate condensations and rarefactions which are propagated in all directions. The impact of a rhythmic succession of such condensations on the ear gives rise to musical sounds; the impact of an arrhythmic or irregular succession gives rise to noises.

If a writing point attached to a tuning-fork in vibration be placed in contact with a traveling recording surface, each vibration will be recorded in the form of a wave. For this reason atmospheric vibrations are generally spoken of as sound-waves. A line drawn horizontally through such a curve indicates the position of rest of the fork; the extent of the curve on each side of this line indicates the excursion of the fork or the amplitude of its movement.

The sensations of sounds which physiologically result from the stimulation of the auditory apparatus are characterized by loudness, pitch and quality or timbre and are the result of the intensity or vigor, frequency, and form of the atmospheric vibrations.

The *intensity* or loudness of a sound depends on the amplitude of the vibration which causes it. The greater the amplitude or swing of the vibrating body, the greater is the energy with which it strikes the ear.

The *pitch* of a sound depends on the number of vibrations which strike the ear in a unit of time—a second. The greater the number, the higher the pitch. Thus while the pitch of the sound caused by the note C, on the first leger line below the G clef, of the music scale, corresponds to 256 vibrations, the pitch of the sound caused by the note C an octave above, corresponds to 512 vibrations. The lowest rate of vibration which can produce a distinct sound varies in different individuals from 14 to 18; the highest rate varies from 35,000 to 40,000 per second. Between these two extremes lies the range of audibility, which embraces about 11 octaves. Vibrations less than 14 per second cannot be perceived as a continuous sound; vibrations beyond 40,000 also fail to be so perceived. In the ascent of the music scale from the lowest to the highest regions there is a gradual increase in the vibration frequency.

The *quality* of a sound depends on the *form* of the vibration. It is this feature which gives rise to those differences in sensations which permit one to distinguish one instrument from another when both are emitting the same note. The form of the sound-wave in any given instance is the resultant of a combination of a fundamental vibration and certain secondary vibrations of subdivisions of the vibrating body. These secondary vibrations give rise to what is known as overtones. By their union with and modification of the fundamental vibration there is produced a special form of vibration which gives rise not to a simple but a composite sensation. It is for this reason that the same note of the piano, the violin, and the human voice varies in quality.

The Function of the Pinna and External Auditory Canal.—In those animals possessing movable ears the *pinna* plays an important part in the collection of sound-waves. In man the pinna plays but a subordinate part in this process. Nevertheless an individual with defective hearing may have the perception of sound increased by placing the pinna at an angle of 90 degrees to the side of the head or by placing the hand behind it. The *external auditory canal* transmits the sonorous vibrations to the tympanic membrane. From the obliquity of this canal it has been supposed that the vibrations, after passing the concha, undergo a series of reflections on their way to the tympanic membrane, which, owing to its inclination, would be struck by them in a much more effective manner.

The Function of the Tympanic Membrane.—The function of the tympanic membrane is the reception of the atmospheric vibrations which are transmitted to it. This it does by vibrating in unison with them. The vibrations which the membrane exhibits correspond in amplitude, in frequency, and in form to those of the atmosphere. That this membrane actually reproduces all vibrations within the range of audibility has been experimentally demonstrated. The membrane, not being fixed as far as its tension is concerned, does not possess a fixed fundamental note, like a stationary fixed membrane, and is. therefore, just as well adapted for the reception of one set of vibrations as another. This is made possible by variations in its tension in accordance with the pitch or frequency of the atmospheric vibrations. In the absence of vibration the membrane is in a condition of relaxation; with the advent of sound-waves possessing a gradual increase of pitch, as in the ascent of the music scale, the tension of the membrane increases until its maximum is reached at the upper limit of the range of audibility. By this change in tension certain tones become perceptible and distinct, while others become imperceptible and indistinct.

The Function of the Tensor Tympani Muscle.—The function of this muscle is, as its name indicates, to change and to fix the tension of the tympanic membrane, so that it can most readily vibrate in unison with vibrations of varying degrees of rapidity. The tendon of this muscle playing around the processus cochleariformis is attached almost at a right angle to the handle of the malleus. Hence as the muscle contracts it exerts its traction from the process and draws the handle of the malleus inward, thus increasing the convexity of the tympanic membrane and at the same time its tension. With the relaxation of the muscle the handle of the malleus passes outward, and the convexity and tension diminish.

In the ascent of the music scale, each note corresponding to an increase in vibration frequency requires for its perception an increase in tension and an increase in the force of the contraction of the tensor muscle. In the descent of the music scale the reverse conditions obtain. The contraction of the muscle is of the nature of a single twitch, and of just sufficient force and duration to tense the membrane for a given rate of vibration.

The contraction of the muscle is excited reflexly. The afferent path is through fibers of the trigeminal nerve distributed to the tympanic membrane; the efferent path is through fibers in the small root of the trigeminal. The stimulus is sudden pressure on the tympanic membrane. The more frequently and forcibly the stimulus is applied, the greater is the muscle response. The tensor tympani muscle may therefore be regarded as an accommodative apparatus by which the tympanic membrane is adjusted for the reception of vibrations of varying degrees of frequency.

The Function of the Chain of Bones.—The function of the chain of bones is to transmit the effects of the atmospheric vibrations to the fluid of the labyrinth. The manner in which this is accomplished becomes evident from the relation which the bones of this chain bear to one another and to the tympanic membrane on the one hand and to the fluid of the labyrinth on the other.

When pressure is made on the outer surface of the tympanic membrane it is at once pushed inward, carrying with it the handle of the malleus, the head at the same time rotating outward around an axis corresponding to its ligamentous attachments. As the handle moves inward a small ledge of bone just below the malleo-incudal joint locks with, and hence pushes inward, the long process of the incus. Since this process is united at almost a right angle to the stapes bone, the latter is forced toward and into the foramen ovale, thus producing a pressure on the perilymph. With the cessation of the pressure the elastic forces of the membrane and of the ligaments return the handle of the malleus to its former position; by the unlocking of the malleo-incudal joint the entire chain also returns to its former position without exerting undue traction on the basal attachment of the stapes.

As the long process of the incus is shorter than the handle of the malleus, and as the movement between them takes place around an axis from before backward, it follows that the excursion of the incus and stapes will be less than that of the malleus, while the force will be greater. Hence as the vibrations are transferred from the tympanic membrane of large area to the base of the stapes of small area (20 to 1.5), they lose in amplitude but increase is force. Their pressure on the perilymph is therefore 13.3 times greater than on the membrana tympani. In addition to its function as a transmitter of vibrations, the chain of bones serves as a point of attachment for muscles which regulate the tension of the tympanic membrane and the pressure on the labyrinth.

The Function of the Stapedius Muscle.—The function of the stapedius muscle is a subject of much discussion. According to Henle, its function is so to adjust the stapes bone that it will be prevented from exerting an undue pressure on the perilymph during the inward excursions of the incus process. According to Toynbee, its function is to press the posterior part of the stapes inward, make it a fixed point, and place the anterior part in such a position that it will vibrate freely and accurately.

The Function of the Eustachian Tube.—In order that the tympanic membrane may vibrate freely it is essential that the air pressure on both sides shall be equal at all times. This is made possible by the Eustachian tube. Were it not for this passageway, with each inward swing of the membrane the air in the tympanic cavity would be condensed and its pressure raised, in consequence of which the movement of the membrane would be retarded; with each outward swing, the air would be rarefied and its pressure lowered below that of the atmosphere, and in consequence the movement outward would be retarded; the maximum response, therefore, of the membrane to a given vibration could not be attained and the resulting sound would be muffled and indistinct. But as with each vibration of the membrane the air can pass into and out of the tympanum through this partially closed tube, inequalities of pressure are prevented and a free vibration permitted.

The impairment in the acuteness of hearing which is caused by either a rise or fall of pressure in the middle ear can be shown—

1. By closing the mouth and nose and then forcing air from the lungs through the Eustachian tube into the tympanum, thus increasing the pressure.
2. By closing the mouth and nose and then making an effort of deglutition. As this act is attended by an opening of the pharyngeal end of the Eustachian tube, the air in the tympanum is partly withdrawn and the pressure lowered. In each instance hearing is impaired. After either experiment the normal condition is restored by swallowing with the nasal passages open.

The Functions of the Internal Ear.—From the anatomic arrangement of the structures of the internal ear it is evident that if the vibrations of the stapes bone are to reach the peripheral organs—the hair cells—of both the vestibular and cochlear nerves, they must traverse successively the perilymph, the membranous walls, and the endolymph. As the perilymph is incompressible, the inward movement of the stapes would be prevented were it not for the elastic character of the membrane closing the foramen rotundum. The pressure wave occasioned by each inward movement of the stapes is transmitted through the scala vestibuli, the helicotrema, and the scala tympani, to this membrane, which by virtue of its elasticity is pressed into the tympanic cavity. With the outward movement of the stapes, equilibrium is at once restored.

The Functions of the Cochlea.—The cochlea is the portion of the internal ear which is concerned in the perception of tones. The arrangement of the histologic elements of the organ of Corti indicates that they in some way respond to the vibrations of varying frequency and form, and through the development of nerve impulses, evoke the sensations of pitch and quality. The manner in which this is accomplished is largely a matter of speculation. While many theories have been offered in explanation of the power to distinguish the pitch and the quality or timbre of a tone, most physiologists prefer that of Helmholtz, who regarded the transverse fibers of the basilar membrane as the elements immediately concerned, and compared them, both in their arrangement and power of sympathetic vibration, with the strings of a piano. He said: "If we could so connect every string of a piano with a nerve-fiber that the nerve-fiber would be excited as often as the string vibrated, then, as is actually the case in the ear, every musical note which affected the instrument would excite a series of sensations exactly corresponding to the pendulum-like vibrations into which the original movements of the air can be resolved; and thus the existence of each individual overtone would be exactly perceived, as is actually the case with the ear. The perception of tones of different pitch would, under these circumstances, depend upon different nerve-fibers, and hence would occur quite independently of each other. Microscopic investigation shows that there are somewhat similar structures in the ear. The free ends of all the nerve-fibers are connected with small elastic particles which we must assume are set into sympathetic vibration by sound-waves" (Stirling).

The mechanism might be regarded, therefore, somewhat as follows: The sound-waves received by the membrana tympani and transmitted by the chain of bones to the fenestra ovalis produce variable pressures in the fluids of the internal ear; these pressures vary in intensity, in number, and in quality, and correspond with the intensity, pitch, and quality of the tones. If, therefore, a compound wave of pressure be communicated by the base of the stapes, it will be resolved into its constituents by the different transverse fibers of the basilar membrane, each picking out its peculiar portion of the wave and thus stimulating corresponding nerve filaments. Thus different nerve impulses are transmitted to the brain, where they are fused in such a manner as to give rise to a sensation of a particular quality, but still so imperfectly fused that each constituent, by a strong effort of attention, may be still recognized. The transverse fibers of the basilar membrane vary in length from 0.04155 mm. at the base of the cochlea to 0.495 mm. at the apex, and, according to Retzius, are about 24,000 in number. As the human ear usually cannot distinguish more than 11,000 tones, it is evident that there is a sufficient anatomic basis for this theory.

The Functions of the Semicircular Canals.—From the pronounced disturbances of equilibrium and progression which follow injury or destruction of one or more of the semicircular canals or of the vestibular branch of the acoustic nerve (phenomena which have been alluded to in connection with a consideration of the functions of the cerebellum (see page 608), it is apparent that they are among the peripheral sense-organs, the physiologic action of which is the development of nerve impulses, which when transmitted to the brain assist the equilibratory mechanism to maintain the equilibrium of the body, both in the standing position and in the various modes of progression. The character of the stimulus, however, and the manner in which it acts on the specialized portion of the sense-organs (the hair cells) is not entirely clear.

In any explanation it must be recalled (1) that the membranous canals are in direct connection with the utriculus, and that both are filled with endolymph; and (2) that these canals act in pairs at least, in the varying positions or movements of the head, *e.g.*, the two horizontal or lateral canals act together when the head is rotated around a vertical axis; the two superior and the two posterior verticals act together when the head is rotated around a horizontal axis; the superior and posterior vertical of one side act together with the corresponding canals of the opposite side when the head is rotated around an antero-posterior or sagittal axis; the superior vertical of one side acts with the posterior vertical of the opposite side when the head is rotated around an oblique axis.

Goltz was the first to present the theory that the stimulus is to be found in the pressure of the endolymph. He stated that in any given position of the head, the endolymph would gravitate to the most dependent portion of the canals and thus press on the nerve endings in one or more of the ampullæ, and thus develop nerve impulses which, when transmitted to the brain, would evoke more or less conscious sensations. These sensations would indicate the position of the head, and lead to the necessary effort to control the movement, to maintain equilibrium and to restore the head to the normal position. If this mechanism is injured this knowledge and this control is interfered with and a want of equilibrium is developed.

Later Breuer propounded the view that the stimulus was to be found in a movement of the endolymph in one or more canals when the head was rotated, a movement which varied in rapidity in proportion to the rate of head rotation. Mach subsequently presented the view that the stimulus was to be found in a variation of pressure, positive or negative in one or more of the ampullæ rather than in an actual movement of the fluid. Crum Brown made the further suggestion that in addition to the movement or pressure of the endolymph there was a movement of the perilymph as well which involved also the walls of the canal. This general theory is usually designated as the *dynamic* in contradistinction to the theory of Goltz which is designated as the *static*. In the dynamic theory, the movement of the fluid in the canal or canals, the plane of which corresponds to the plane in which the head is rotated, though in the opposite direction, is over the hair cells at the ampullæ and thus acts as a stimulus. Thus, if the head is rotated to the right around a vertical axis and in a horizontal plane the endolymph in the right half of each horizontal or lateral canal will flow toward the ampulla, and in the left half away from the ampulla. If the head is rotated to the left the reverse movements would arise.

If the head is rotated backward around a horizontal axis the endolymph will flow in both posterior vertical canals in the opposite direction, *i.e.*, away from the ampullæ and if the head is rotated around the same axis forward, the reverse movement takes place. If the head is rotated around an oblique axis, the endolymph will flow in the superior vertical canal of one side away from the ampulla and in the posterior vertical canal of the other side toward the ampulla. Thus whatever the plane of rotation of the head may be, there is always a flow of endolymph in the opposite direction, which movement, or variation in pressure, becomes the effective stimulus. The nerve impulses developed by this stimulation when transmitted to the brain evoke more or less conscious sensations, which inform us as to the direction and the extent of movement of the head and calls forth the action of the mechanism by which the movement is regulated and controlled and the equilibrium of the body maintained.

CHAPTER XXXI

REPRODUCTION

Reproduction is the process by which a new individual is initiated and developed and the species to which it belongs is preserved. Reproduction is the result of the union and subsequent development of germ- and sperm-cells. These cells are produced and their union accomplished by the coöperation of the reproductive organs characteristic of the two sexes.

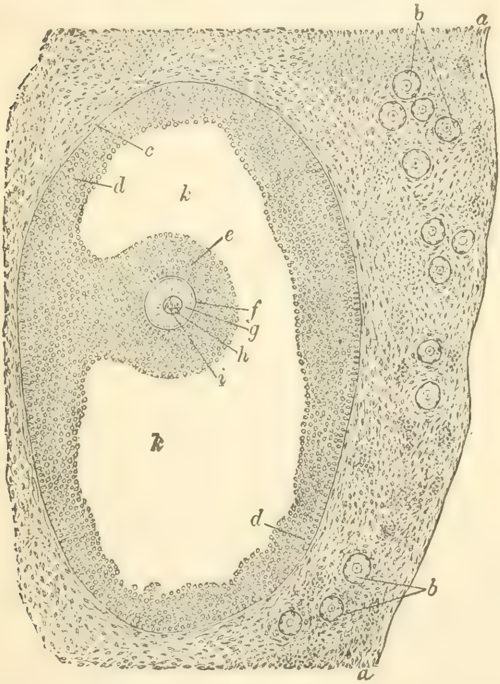

FIG. 326.—SECTION OF CORTEX OF CAT'S OVARY, EXHIBITING LARGE GRAAFIAN FOLLICLES. *a*. Peripheral zone of condensed stroma. *b*. Groups of immature follicles. *c*. Theca of follicle. *d*. Membrana granulosa. *e*. Discus proligerus. *f*. Zona pellucida. *g*. Vitellus. *h*. Germinal vesicle. *i*. Germinal spot. *k*. Cavity of liquor folliculi.—(*After Piersol.*)

Embryology is a department of anatomic science which has for its object the investigation of the successive stages that the new being passes through during its gradual development prior to birth.

THE REPRODUCTIVE ORGANS OF THE FEMALE

The reproductive organs of the female comprise the ovaries, Fallopian tubes, uterus, and vagina.

The Ovaries.—The ovaries are two small, flattened bodies, measuring about 40 mm. in length and 20 in breadth. They are situated in the cavity of the pelvis, one on either side, and embedded in a fold of the peritoneum, known as the broad ligament. A section of the ovary shows that it consists externally of a thin, firm, connective-tissue membrane and internally of a fine connective-tissue stroma, supporting blood-vessels, non-striated muscle-fibers and nerves, and containing in its meshes a very large number of spheric sacs named after their discoverer, de Graaf, the *Graafian sacs* or *follicles*. These follicles are very numerous and are present in all portions of the ovary, though they are most abundant toward its peripheral portions. It is estimated that each human ovary contains from 20,000 to 40,000 follicles. The follicles vary considerably in size;

while many are visible to the unaided eye, others require for their detection high powers of the microscope. Although the follicles are present in the ovary at the time of birth, it is not until the period of puberty that they assume functional activity.

From this time on to the catamenial period there is a constant growth and development of these follicles. Each follicle consists of an external investment of fibrous tissue and blood-vessels, and an internal investment of cells, the *membrana granulosa*. At the lower portion of this membrane there is an accumulation of cells, the *proligerous disc* (Fig. 326). The cavity of the follicle contains a slightly yellowish, alkaline, albuminous fluid, a transudate in all probability from the blood-vessels. The Graafian follicle is of especial interest, for it is in this structure, and more especially in the proligerous disc, that the true germ-cell or ovum is developed.

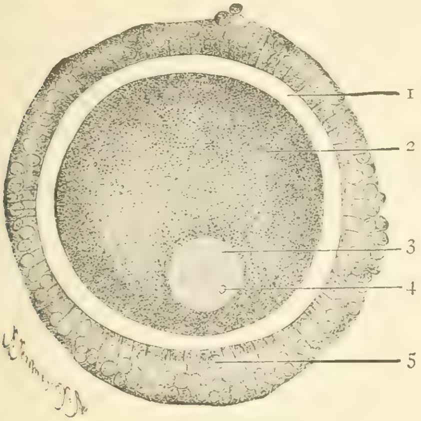

FIG. 327.—OVUM OF A COW. 1. Zona pellucida. 2. Cytoplasm, vitellus. 3. Nucleus, germinal vesicle. 4. Nucleolus, germinal spot. 5. Corona radiata. The radial striation of the zona pellucida cannot be seen.—(*Stöhr.*)

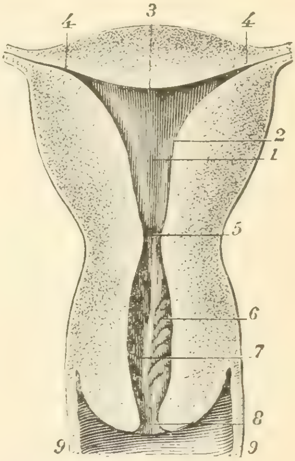

FIG. 328.—FRONTAL SECTION OF THE UTERUS. 1. Cavity of the body. 2, 3. Lateral walls. 4, 4. Cornua. 5. Os internum. 6. Cavity of the cervix. 7. Arbor vitæ of the cervix. 8. Os externum. 9. Vagina.—(*Sappey.*)

The **ovum** is a spheric body measuring about 0.3 mm. in diameter. It consists of a mass of living, protoplasmic material, *cytoplasm*, a *nucleus* or *germinal vesicle*, and a *nucleolus* or *germinal spot*. The cytoplasm presents toward its central portion a quantity of granular material, partly fatty in character, the *deutoplasm* or *vitellus*. The peripheral portion of the cytoplasm is surrounded by a clear thick membrane, the *zona pellucida*, external to which is a layer of radially placed columnar epithelium, the *corona radiata* (Fig. 327).

The *nucleus* consists of a nuclear membrane enclosing contents. The latter consist of an amorphous material in which is embedded a network, some of the threads of which have a strong affinity for certain staining materials, and hence are known as *chromatin*, in the meshes of which lies a material that stains less deeply and known as *achromatin*.

The Fallopian Tubes.—The Fallopian tubes are about 12 centimeters in length and extend from the upper angles of the uterus to the ovaries. Each tube is somewhat trumpet-shaped, the narrow portion being close to the uterus, the wide portion close to the ovary. The outer extremity of the tube is expanded and subdivided, and presents a series of processes termed fimbriæ, one of which is attached to the ovary. The tube consists of three coats—an external or fibro-serous; a middle or muscle, the fibers of which are arranged longitudinally and circularly; and an internal or mucous, which is folded longitudinally. The surface of the mucous coat is covered with a layer of ciliated epithelial cells, the direction of motion of which is toward the uterus.

The Uterus.—The uterus is pyriform in shape and divided into a body and neck. It measures, before the first pregnancy, about 7 cm. in length, 5 cm. in breadth and 2½ cm. in thickness. A frontal section of the uterus shows a central cavity which in the body is triangular in shape, in the neck oval or fusiform (Fig. 328). At the upper angles of the uterus the cavity is continuous with the cavity of each Fallopian tube. At the junction of the body and the neck, the cavity presents a constriction, *the internal os*. The constriction at the end of the neck is known as the *external os*. The walls of the uterus are extremely thick and composed of non-striated muscle-fibers arranged in a very complicated manner. The interior of the uterus is lined by mucous membrane covered with cylindric ciliated epithelial cells, the motion of which is toward the external os. Tubular glands are found in large numbers in the mucous membrane lining the cavity, while racemose glands are found in the mucous membrane lining the neck. Owing to the flattening of the uterus from before backward the walls are almost in contact and the cavity almost obliterated.

The Vagina.—The vagina is a musculo-membranous canal, from 12 to 18 cm. in length, situated between the rectum and bladder. It extends from the surface of the body to the brim of the pelvis, and embraces at its upper extremity the neck of the uterus.

Ovulation.—After the establishment of puberty a Graafian follicle develops and ripens or matures periodically, usually every twenty-eight days. During the time of maturation the follicle increases in size, from an augmentation of its fluid contents, and approaches the surface of the ovary, where it forms a projection varying from 6 to 12 mm. in size. When maturation is complete the vesicle ruptures, and the ovum and liquid contents are discharged. The ovum, by a mechanism not fully understood, is received by the fimbriated extremity of the Fallopian tube and enters its cavity. The ovum is then transferred through the tube by the peristaltic contraction of its muscle-fibers and by the action of the cilia of its lining epithelium. The time occupied in the transference of the ovum from the ovary to the interior of the uterus has been estimated to be from four to ten days.

Either at the time of, or very shortly after, its discharge from the follicle, the ovum, and more especially the nucleus, undergoes a series of histologic changes which eventuates in an extrusion of a portion of the chromatin material. The extruded portions are known as the polar bodies. The non-extruded portion of the chromatin material is known as the female *pronucleus* or *germ nucleus*. The chromosomes are reduced to one-half the somatic number. The succession of changes which the nucleus undergoes is termed maturation. As the nucleus is regarded as the part of the ovum which transmits parental characteristics it is assumed that the extrusion of a portion of the nuclear material is a means by which an excess of inherited substance is prevented.

Menstruation.—Menstruation is a periodic discharge of blood and mucus from the surface of the mucous membrane of the uterus, and occurs about every twenty-eight days. The duration of the menstrual period extends over four or five days and the amount of blood discharged varies from 180 c.c. to 200 c.c. Menstruation is usually an accompaniment of ovulation, though the latter process may take place independently of the former. It is characterized by both local and systemic changes. The local changes are most marked in the uterus, the mucous membrane of which increases in thickness from a proliferation of the connective tissue and a hyperemic condition of the blood-vessels. Subsequently to these changes the epithelial surface, as well as the more superficial portions of the connective tissue, undergo degeneration and exfoliation, after which the finer blood-vessels rupture and permit of an escape of blood into the uterine cavity. At the end of the menstrual period regenerative changes set in which continue until the normal condition of the mucous membrane is reëstablished.

The Corpus Luteum.—With the rupture of the Graafian follicle there is an effusion of blood into the follicular cavity which soon coagulates, loses its color and assumes the characteristics of fibrin. The walls of the follicle, which have become thickened from the deposition of a reddish-yellow glutinous substance, now become convoluted and undergo a still further hypertrophy, until they encroach upon and almost obliterate the follicular cavity. In a few weeks the mass loses its red color and becomes decidedly yellow, when it is known as the *corpus luteum.* With the continuance of reparative changes this body gradually disappears until at the end of two months nothing remains but a small cicatrix on the surface of the ovary. Such are the changes in the follicle if the ovum has not been impregnated.

The corpus luteum, after impregnation has taken place, undergoes a much slower development, becomes larger, and continues during the entire period of gestation. The difference between the corpus luteum of the unimpregnated and pregnant condition is expressed in the following table by Dalton:

	Corpus Luteum of Menstruation.	Corpus Luteum of Pregnancy.
At the end of three weeks.	Three-quarters of an inch in diameter; central clot reddish; convoluted wall pale.	
One month..........	Smaller; convoluted wall bright yellow; clot still reddish.	Larger; convoluted wall bright yellow; clot still reddish.
Two months........	Reduced to the condition of an insignificant cicatrix.	Seven-eighths of an inch in diameter; convoluted wall bright yellow; clot perfectly decolorized.
Four months........	Absent or unnoticeable........	Seven-eighths of an inch in diameter; clot pale and fibrinous; convoluted wall dull yellow.
Six months..........	Absent......................	Still as large as at the end of second month; clot fibrinous; convoluted wall paler.
Nine months..... ...	Absent..................	Half an inch in diameter; central clot converted into a radiating cicatrix; external wall tolerably thick and convoluted, but without any bright yellow color.

THE REPRODUCTIVE ORGANS OF THE MALE

The reproductive organs of the male comprise the testicles, vasa deferentia, vesiculæ seminales, and penis.

The Testicles.—The testicles are oblong glands, about 40 mm. in length, 30 mm. in breadth and 20 mm. in thickness, and contained within the cavity of the scrotum. A section of the testicle (Fig. 329) reveals the presence externally of a dense fibrous membrane, the *tunica albuginea*, and internally a connective-tissue framework consisting mainly of septa, which enter the organ on its posterior aspect at the *mediastinum testis*, passing inward in a diverging manner. The spaces between the septa are occupied by the true gland substance, the seminiferous tubules.

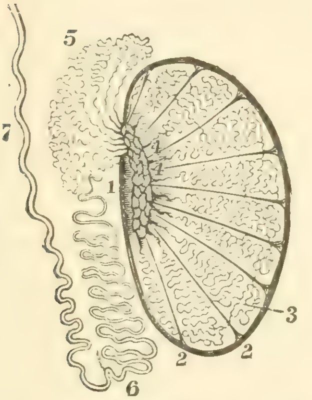

Fig. 329.—Diagram of a Vertical Section through a Testicle. 1. Mediastinum testis. 2, 2. Trabeculæ. 3. One of the lobules. 4, 4. Vasa recta. 5. Globus major of the epididymis. 6. Globus minor. 7. Vas deferens.—(*Holden.*)

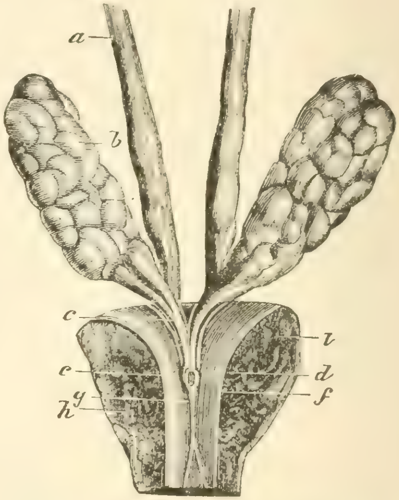

Fig. 330.—Vas Deferens, Vesiculæ Seminales, and Ejaculatory Ducts. *a.* Vas deferens. *b.* Seminal vesicle. *c.* Ejaculatory duct. *d.* Termination of the ejaculatory duct. *e.* Opening of the prostatic utricle. *f, g.* Veru montanum. *h, l.* Prostate.—(*Liégeois.*)

The seminiferous tubules are very numerous, the estimate as to their number varying from 800 to 1000. When unraveled they measure from 30 to 40 cm. in length and 0.3 mm. in diameter. At their peripheral extremities the tubules are very much convoluted, but as they pass toward the mediastinum testis, the convolutions disappear, and after uniting with one another terminate in from twenty to thirty straight tubes, of small diameter, the *vasa recta*, which pass through the mediastinum and form the *rete testis*. At the upper part of the mediastinum the tubules unite to form from nine to thirty small ducts, the *vasa efferentia*, which soon become very much convoluted. After a short course they unite to form a single tortuous tube, about 7 meters in length and 0.4 mm. in diameter, which descends behind the testicle to its lower border. This tube is known as the epididymis. The seminal tubule consists of a basement membrane lined by granular nucleated epithelium.

The *vas deferens*, the excretory duct of the testicle, is about 60 cm. in length and from 2 to 3 mm. in diameter, and extends upward from the epididymis to the inguinal canal, through which it passes into the abdominal cavity and then to the under surface of the base of the bladder, where it unites with the duct of the vesicula seminalis to form the *ejaculatory duct.*

The **vesiculæ seminales** are two lobulated pyriform bodies, about 40 mm. in length, situated on the under surface of the bladder. Each vesicula seminalis consists of an external fibrous coat, a middle, muscular coat, and an internal mucous coat. The mucous coat contains a number of small tubular albumin-producing glands which secrete a characteristic fluid.

The *ejaculatory duct*, formed by the union of the vas deferens and the duct of the *vesicula seminalis*, opens into the prostatic portion of the urethra (Fig. 330).

The **prostate gland** is a musculo-glandular mass surrounding the posterior extremity of the urethra. It contains a large number of tubules. more or less branched and convoluted, and lined by columnar epithelium, They secrete a fluid which is poured into the urethra at the time of the ejaculation of semen and impart motility to the spermatozoa or spermia.

The **penis** consists of three parts: the *corpus spongiosum* below, through which passes the urethra, and the two *corpora cavernosa*, one on either side and above. The corpus spongiosum terminates anteriorly in a conic-shaped structure, the *glans penis;* the corpora cavernosa consist externally of a fibrous investment and internally of a fibrous investment and internally of erectile tissue. These bodies are abundantly supplied with blood, which after entering their substance by the arteries, passes into sinuses or reservoirs, from which it is carried away by veins. These vessels pass to the dorsum of the penis and unite to form a large vein by which the blood is returned to the general circulation. By virtue of the erectile tissue in the corpora cavernosa the penis becomes erect and rigid when the blood supply is increased. This takes place in response to peripheral stimulation or emotional states, or both combined. When these conditions are established nerve impulses pass outward through nerves, the *nervi erigentes*, which have their origin in the lumbar segment of the spinal cord, and bring about an active dilatation of the arteries and a relaxation of the non-striated muscle-fibers in the corpora cavernosa. (See page 380.) With these events there is a rapid influx of blood and a distention and an erection of the organ. This condition is furthered and maintained by a partial compression of the dorsal vein by the fibrous capsule.

Semen.—The semen is a complex fluid composed of the secretions of the testicles, the vesiculæ seminales, the prostatic tubules, and urethral or Cowper's glands. It is grayish-white in color, mucilaginous in consistency, characteristic in odor, and somewhat heavier than water. In response to appropriate stimulation the muscle-fibers in the walls of the vasa deferentia, vesiculæ seminales, and prostatic tubules contract and discharge their contents into the urethra, from which they are forcibly ejected by the rhythmic contraction of the ejaculatory muscles, the *ischio-* and *bulbo-cavernosi.* The amount of semen discharged at each ejaculation varies from 1 to 5 c.c.

Spermatozoa.—The spermatozoa or spermia are peculiar morphologic elements which arise within the seminiferous tubules as a result of complex histologic changes in the lining epithelium. An adult spermatozoön consists of a conoid slightly flattened head, from the posterior part of which there projects a short straight rod, provided with a long filamentous tail or cilium and an end-piece (Fig. 331). The head contains a nucleus of chromatin material. The total length of a spermatozoön varies from 50 to 80 micro-millimeters. The characteristic physiologic feature of spermatozoa is incessant locomotion when in a suitable medium. So long as they are confined to the vas deferens they are quiescent, but with their advent into the vesicula seminalis and dissemination in its contained fluid, they become extremely active and move around with considerable rapidity. The power of locomotion depends on the possession of the tail which, by lashing the surrounding fluid now in this and now in that direction, propels the head from place to place. The vitality of spermatozoa is such as to enable them to retain their physiologic activities in the uterus for more than eight days.

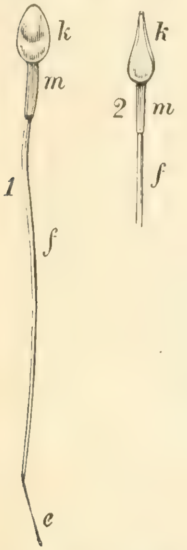

FIG. 331.—HUMAN SPERMATOZOÖN. 1. Front view, 2, side view, of the head. *k*. Head. *m*. middle piece. *f*. Tail. *e*. Terminal filament.—(*After Retzius.*)

The development of spermatozoa from testicular cells as observed in lower animals indicates that each cell gives rise to four embryonic forms—spermatids —which subsequently develop into adult spermatozoa. In this process the primary nuclear chromatin undergoes a division, so that each spermatozoön receives but a fractional amount representing one-half the number of somatic chromosomes. The changes by which this condition is brought about are comparable to the changes exhibited by the ovum, and have for their result a reduction in the quantity of hereditary substance to be transmitted.

Fecundation.—Fecundation is the union of the spermatozoön (the sperm-cell) with the ovum (the germ-cell) and takes place in the great majority of instances in the Fallopian tube. After the introduction of the spermatozoa into the vagina during the act of copulation, they soon begin to pass upward, into and through, the uterine cavity and out into the Fallopian tube, where they accumulate in large numbers and retain their vitality for some days. The migration is effected by the propelling power of the filamentous tail and by the action of the cilia of the uterus and tubes.

From observations made on the behavior of the spermatozoa toward the ovum in lower animals, and on the manner in which their union is effected, the inference may be drawn that a similar procedure takes place in mammals. In lower animals the spermatozoa on approaching an ovum take on increased activity, swimming around it in all directions and apparently seeking a point of entrance. In fish and molluscs the zona pellucida presents a distinct opening, the *micropyle*, through which the spermatozoön passes. Inasmuch as the mammalian ovum is devoid of such an opening, the mechanism of entrance of the spermatozoön is not clearly understood. Notwithstanding their enormous numbers it is generally believed that but a single spermatozoön effects an entrance into the ovum. With the accomplishment of this, however, the spermatozoön loses its mobility, after which the tail disappears.

The germ nucleus proceeds to the middle of the ovum where it is followed by head and middle-piece of the spermium; the middle-piece forms a central spindle while the germ nucleus and head of the spermium each resolves itself into one-half the number of chromatic loops of a somatic cell. In this condition the fertilized ovum represents a parent cell, that possesses the physiologic activities and characters of both ancestral cells. From this parent cell the offspring develops through successive division, multiplication and differentiation of the resulting cells. The chromatic material of the germ nucleus and head of the spermium represent the transmitters of inherited characters.

The Fixation of the Ovum.—The ovum, after fertilization in the oviduct, continues to divide and pass slowly to the uterus (8 to 10 days) where it is retained until the end of gestation. A menstrual mucosa having developed the ovum lodges on a smooth thick area and gradually sinks beneath the surface. During the passage down the oviduct the zona pellucida has become attenuated and has been finally replaced by a thick layer of ameboid and phagocytic cells called the *trophoderm.* Upon lodgment of the ovum these cells destroy the underlying mucosa and produce a cavity into which the ovum sinks. As the ovum increases in size the mucosa gradually covers it; that portion of the mucosa toward the uterine cavity is called the *decidua capsularis* (*d. reflexa*), that beneath the ovum the *decidua basilaris* (*placental d.*), while the remainder constitutes the *decidua parietalis* (*d. vera*). As development proceeds the decidua basilaris becomes greater, ultimately developing into the placenta.

Segmentation of the Ovum.—Immediately after fertilization the ovum divides and redivides, within the diminishing zona pellucida, forming an irregular mass called the *morula.* The peripheral cells form a layer, the *trophoderm,* beneath the attenuated zona pellucida ultimately replacing that structure. The remaining cells of the morula differentiate into three masses—*ectodermal*, *entodermal* and *mesodermal;* the central cells of these masses liquefy and disappear forming thus the *ectodermal* or *amniotic* cavity, limited by the ectoderm; the *entodermal* cavity, limited by the entoderm; and the *mesodermal* or *celomic* cavity, limited by the extra-embryonic mesoderm. Meanwhile cells in various parts of the thickened trophoderm have disappeared leaving this layer in the form of delicate trophodermal villi, the future chorionic and placental villi.

The Embryonic Shield.—The floor of the amniotic cavity, consisting of ectoderm and entoderm, constitutes the *embryonic shield* or *disc.* As the shield increases in size a median longitudinal thickening is seen occupying the caudal half of the area. This is the *primitive streak,* a temporary structure that is soon overshadowed by changes in the areas just in front of it. Here is formed a median, longitudinal, grooved ridge of ectoderm, that develops rapidly in length. This is the *neural* groove and *folds.* The dorsal lips of the groove approach each other in the mid-line and fuse, separating from the original ectoderm which closes over the ectodermal tube. This ectodermal tube is the *neural tube* from which the nerve system is developed.

In the immediate vicinity of the head end of the primitive streak is seen a darkened area, *Hensen's node* that represents the beginning invagination of the ectoderm in the formation of the embryonic mesoderm and notochord to be considered later. That portion of the embryonic shield that gives rise to the embryo itself becomes distinctly outlined laterally and in the head and tail regions of the neural groove. Just external to this area, the *embryonic area proper*, is a transparent area, the *area pellucida*, beyond which is the *area opaca* in which the first blood-vessels appear.

Mesoderm and Notochord.—So far in the embryonic area only ectoderm and entoderm exist. Hensen's node at the head end of the primitive streak represents an invagination (gastrulation) of ectoderm between ectoderm and entoderm. This invagination elongates headward in the embryonic area constituting a tube of ectodermal cells, the *chordal canal.* Later the ventral wall of the canal and the adjacent entoderm disappear so that the chordal ectoderm temporarily forms the dorsal median boundary of the entodermal cavity. By this process a communication is established between the entodermal cavity and neural groove, called the *neurenteric canal.* The chordal ectoderm separates from the entoderm and then forms a solid cord of cells, *the notochord*, between entoderm and neural groove, the neurenteric canal, however, persisting for some time. In the meantime other ectodermal cells in the region of the chordal invagination spread between ectoderm and entoderm and form the *anlage of the mesoderm.* These cells by rapid proliferation soon separate ectoderm and entoderm and join the extra-embryonic mesoderm. The separation of ectoderm and entoderm is complete except in the regions of the *bucco-pharyngeal* and *cloacal membranes.*

Upon each side of the neural groove the mesoderm becomes transversely grooved on its ectodermal surface, forming a number of successive block-like masses called *primitive somites* or *segments.* Of these there are thirty-eight of the trunk and possibly four for the head region. Each segment consists of three parts—the *sclerotome*, the *myotome* and the *dermatome.* Lateral to the somite is a thickened mass of mesoderm, *the intermediate cell-mass*, that laterally splits into two layers, the outer accompanies the ectoderm forming the *somatopleure* which gives rise to the body-wall, the inner joins the entoderm forming the *splanchnopleure* from which the gut-tract, vitelline duct and yolk-sac are derived.

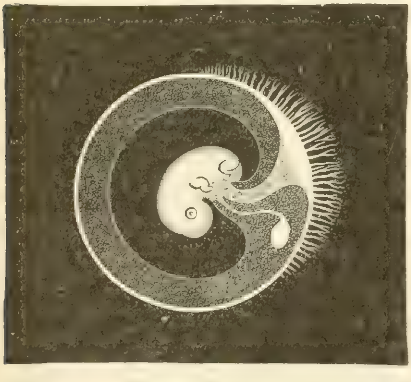
FIG. 332.—HUMAN EMBRYO AND ITS ENVELOPES AT THE END OF THE THIRD MONTH. —(*Dalton.*)

Fetal Membranes.—As the primitive streak and neural groove are forming, the extra-embryonic mesoderm that lies beneath the trophoderm invades the trophodermal villi forming thus the *chorion* with its *villi.* Gradually the mesoderm of the roof of the amniotic cavity splits into two layers, the upper constituting chorionic mesoderm while the under one attached to the ectoderm of the amniotic forms with the latter the *amnion.* In the chick and some mammals, the amnion is derived from the somatopleure in the folding off of the body. In amniotes the amniotic cavity is at first small but rapidly increases in size. It contains a clear, transparent liquid, the *amniotic fluid*, which amounts to about one liter at term; it serves to protect the fetus during gestation and at parturition it dilates the os cervicis, and flushes the birth canal. This liquid is derived mainly from the blood as it contains albumin, sugar, fat and inorganic salts. Traces of urea indicate that some of its constituents are derived from the embryo itself.

The caudal end of the embryonic area is left connected with the chorion by a heavy band of mesoderm termed the *belly-stalk*, to which the caudal part of the amnion is attached. The entoderm is invaginated into the belly-stalk for a short distance constituting the *allantois* of higher forms. In oviparous forms the allantois grows out between the closing somatopleuric folds that form the body-wall and constitutes a free sac upon which vessels (*allantoic arteries* and *veins*) develop from the embryo. This sac then spreads beneath the white shell membrane forming the organ of nutrition and respiration of these forms during the last half of their incubation periods. In mammals the extra-embryonic portion of the allantois is of little importance (Fig. 332).

Placenta Formation.—The chorionic villi increase rapidly in size and number and usually surround the whole fetal sac, giving it a peculiar shaggy appearance. Blood-vessels now proceed from the embryo along the belly-stalk (not the allantois in higher forms as formerly stated). These, the *umbilical arteries* and *veins*, pass to the chorionic villi and send branches to those of the placental area; these vascularized villi constitute the *chorion frondosum*, while the avascular villi form the *chorion leve*. The villi of the latter disappear during the second month, leaving the chorionic membrane smooth. The villi of the chorion frondosum now penetrate the uterine glands of the decidua basilaris, which by this time have been denuded of epithelium, and have gained connection with the blood-vessels of the mucosa; in this manner these uterine glands have become converted into blood sinuses. The chorionic villi either attach themselves to the tunica propria of the mucosa

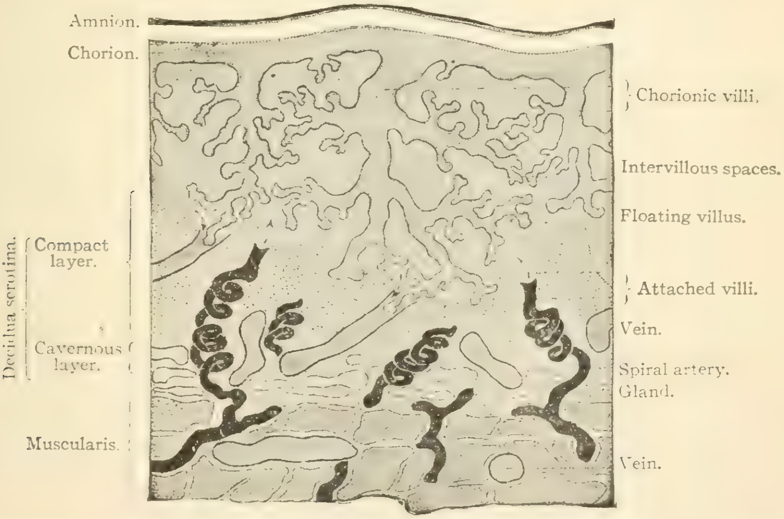

FIG. 333.—DIAGRAM OF HUMAN PLACENTA AT THE CLOSE OF PREGNANCY.—(*Schaper.*)

(*fixed villi*) or remain free (*floating villi*). At the edge of the placental area very few villi develop, leaving a circular channel called the *marginal sinus*. This attachment of villi becomes marked from the third month on and this is considered the beginning of placentation. From this time on to term there is merely an increase in number of villi and vessels with thus a corresponding increase in the size of the placenta. (Fig. 333.)

The Placenta.—Of all the embryonic structures the placenta is the most important. It is formed by the end of the third month, after which it gradually increases in size up to the end of the eighth month, by which time it is fully developed. It then measures from 18 to 24 cm. in diameter and weighs from 400 to 600 grams. It is most frequently attached to the upper and back part of the uterine wall. Though exceedingly complex in structure it consists essentially of two portions, a fetal and a maternal.

The *fetal* portion consists primarily of those villi on the chorion in relation with the decidua basilaris. These structures gradually increase in size and number, and receive the ultimate branches of the umbilical arteries. The *maternal* portion consists primarily of the decidua basilaris. As gestation advances the placental villi rapidly increase in size and number, and receive the branches of the umbilical arteries. At the same time the decidua basilaris becomes hypertrophied and vascular. With the continued growth and development of these two structures they gradually fuse together and finally become inseparable. In accordance with the needs of the embryo, the decidua basilaris and its contained blood-vessels undergo certain histologic changes which result in the formation of large cavities, sinuses, or lakes, into which the blood of the uterine vessels is emptied. As the placenta develops, the structures separating the blood of the mother from that of the child gradually become modified until they are represented by a thin cellular or homogeneous membrane. The conditions now are such as to permit of a free exchange of material between the mother and child. Whether by osmosis or by an act of secretion, the nutritive materials of the maternal blood pass through the intervening membrane into the fetal blood on the one hand, while waste products pass in the reverse direction into the maternal blood on the other hand. Inasmuch as oxygen is absorbed and carbon dioxid exhaled by the same structures, the placenta is to be regarded as both an absorptive and a respiratory organ. So long as these exchanges are permitted to take place in a normal manner the nutrition of the embryo is secured.

The Nutritive Supply of the Embryo.—The growth and development of the embryo from the period of fertilization to the period of birth require a continuous and ever increasing supply of food materials. This is derived from several sources and requires for its utilization, the development, in different classes of animals, of specialized forms of the circulatory apparatus, the relative importance of which varies in accordance with the source of the food supply. These are known as the vitelline, the allantoic, and the placental circulations. All these forms are present at successive stages in the development of the human embryo but only the last is of major importance.

As the ovum passes down the oviduct it imbibes its nutritive material from the mucosa. When it lodges itself in the uterus it probably receives additional material in the same way. The period during which it does so is, however, very limited.

The *Vitelline Circulation.*—The vitelline circulation, which in oviparous animals, *e.g.*, the chick, is of primary importance because of the large amount of food stored in the vitellus or yolk, is in mammals of relatively slight importance because of the limited supply of food in the vitellus. It is nevertheless present in early stages.

The *Allantoic Circulation* which in oviparous animals is also of primary importance in the latter half of the incubation period both as an absorption and respiratory apparatus is also present in mammals to a slight extent, but it is merely a transition stage in the development of placental circulation.

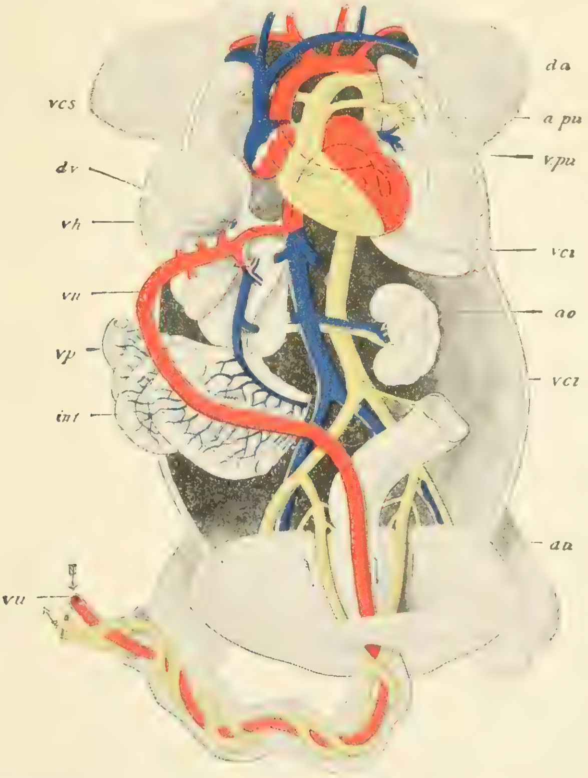

FIG. 334.—THE FETAL CIRCULATION. *ao.* Aorta. *a.pu.* Pulmonary artery. *au.* Umbilical artery. *da.* Ductus arteriosus. *dv.* Ductus venosus. *int.* Intestine *vci* and *vcs.* Inferior and superior venæ cavæ. *vh.* Hepatic vein. *vp.* Venaportæ. *v. pu.* Pulmonary vein. *vu.* Umbilical vein.—(*From Kollmann.*)

The Placental Circulation.—The development of the fetal or placental circulatory apparatus by which the fetus obtains its food supply and necessary oxygen and frees itself from carbon dioxid has been alluded to in a foregoing paragraph relating to the formation of the placenta. After the blood-vessels of the embryo, the umbilical arteries and vein have come into histologic and physiologic relations with the uterine blood-vessels, the nutritive materials and the oxygen are derived entirely from the maternal blood-stream which at the same time receives carbon dioxid and perhaps other waste products from the fetal blood-stream. The placenta thus serves as a digestion and respiratory organ. The blood having undergone these changes now leaves the placenta and returns to the fetus by the umbilical vein. This blood is relatively rich in nutritive material and of a scarlet red color by reason of the presence of an increased amount of oxygen. As it passes into the abdominal cavity a portion, about one-half, of the blood is directed by the *ductus venosus* into the inferior vena cava, while the remainder is emptied into the portal vein, by which it is distributed to the liver and from which it emerges by the hepatic veins and is poured into the inferior vena cava. The blood in the vena cava is thus a mixture of venous blood from the lower extremities and liver, and oxygenated blood from the placenta. After its discharge into the right auricle the blood is directed by a fold of the lining membrane, the Eustachian valve, through an opening in the interauricular septum, the *foramen ovale*, into the left auricle. It then flows through the auriculo-ventricular opening into the left ventricle, thence into the aorta, and by its branches is distributed to all parts of the body.

The blood from the head and upper extremities is emptied by the superior vena cava into the right auricle, but as it passes in front of the Eustachian valve, it flows directly into the right ventricle and then into the pulmonary artery. On account of the unexpanded condition of the lungs and the almost impervious condition of the pulmonary capillaries, but a small portion of the blood passes through them, while the larger portion by far passes into the aorta directly through a duct, the *ductus arteriosus*, which enters at a point below the origin of the left carotid and subclavian arteries. A comparison of the blood distributed to the head and upper extremities, with that distributed to the lower extremities, will show a larger percentage of nutritive material and oxygen in the former than in the latter, a fact which has been offered as an explanation of the more rapid growth of the liver and upper half of the body. As the blood passes through the aorta, a portion is directed from the main current by the hypogastric and umbilical arteries to the placenta, where it loses carbon dioxid and gains oxygen, and changes in color from a bluish red to a scarlet red.

Parturition.—At the end of gestation—approximately 280 days from the time of conception—a series of changes occur in the uterine structures which lead to an expulsion of the child, the placenta, and decidua vera. To this process in its entirety the term parturition is given. At this time, from causes not clearly defined, the uterine walls begin to exhibit throughout their extent a series of slight contractions which are somewhat peristaltic in character; these contractions, which gradually increase in frequency and vigor, bring about a dilatation of the internal os and a descent of the membranes into the cervical canal. The pressure exerted by these membranes during the time of the contraction materially assists in the relaxation of the circular fibers and a dilatation of the external os. When the dilatation has so far advanced that the diameter of the external os attains a measure of 7 or 8 cm., the tension of the membranes becomes sufficiently great to lead to their rupture and to a partial escape of the amniotic fluid. With this event, the presenting part of the child, usually the head, descends into the vagina. After a short period of rest the uterine contractions return and rapidly increase in vigor and duration. As a result of the pressure thus exerted from all sides on the body of the child, the head gradually descends still further into the vagina and finally emerges through the vulva to be followed in a short time by expulsion of the trunk and limbs, and a discharge of the remaining amniotic fluid. With the expulsion of the child the uterine contractions cease for a period of ten or fifteen minutes, when they again recur, with the result of detaching the placenta and expelling it into the vagina. It is then removed by the coöperative action of the abdominal and perineal muscles. The hemorrhage which would naturally occur with the detachment of the placenta and the laceration of the maternal vessels is prevented by the firm continuous contraction of the uterine walls, by which the vessels are compressed and permanently closed.

The Establishment of Inspiration and the Adult Circulation.—After the birth of the child and the detachment of the placenta, there speedily occurs a decrease in the quantity of oxygen and an increase in the quantity of carbon dioxid in the blood, a condition which causes a discharge of nerve energy from the inspiratory center, a contraction of the inspiratory muscles, an expansion of the thorax, and an inflow of air into the lungs.

In addition it is very probable that the stimulation of the inspiratory center is also occasioned by the arrival of nerve impulses from the skin, developed by the cooling of the skin due to the vaporization of the amniotic fluid.

In the later months of intrauterine life the vascular apparatus undergoes certain anatomic changes which favor the transition from the placental to the adult circulation. Thus the *ductus venosus* contracts, and sends a a larger volume of blood into and through the liver; the Eustachian valve diminishes in size and at the time of birth has almost disappeared; a membranous fold grows upward and backward from the edge of the foramen ovale on the left side; the *ductus arteriosus* also contracts. With the first inspiration and the expansion of the lungs, the blood which enters the pulmonary artery passes through the pulmonary capillaries in large volume and is returned by the pulmonary veins to the left auricle. The entrance of the blood into this cavity presses the membranous fold against the margins of the foramen ovale and thus prevents the further flow of blood from the right auricle. The blood entering the right auricle by the inferior vena cava now flows into the right ventricle, which is favored by the small size of the Eustachian valve. The foramen ovale is permanently closed at the end of a week or ten days; the ductus arteriosus at the end of four days. The umbilical vein and ductus venosus, at the end of four or five days, have also become almost impervious from the contraction of their walls. The proximal ends of the hypogastric arteries remain open and carry blood to the walls of the bladder. The distal ends of the arteries are converted into impervious cords.

Lactation.—As pregnancy advances the mammary glands increase in size, partly from a deposition of fat and connective tissue and partly from a multiplication of the secreting acini. The lining epithelial cells at the same time increase in size, and toward the end of pregnancy begin to exhibit functional activity. At the time of birth, or within a day or so after birth, the acini are filled with a fluid which in its qualitative composition resembles milk and is known as *colostrum*. It is distinguished from milk more especially in the fact that it contains in large quantity a proteid which coagulates on boiling, and certain inorganic salts which have a laxative effect on the new-born child. Normal lactation and the phenomena which accompany it are fully established by the end of the second or third day.

The composition of milk and the mechanism of its production have been stated in the chapter on Secretion.

Physiologic Activities of the Embryo.—During intrauterine life the evolution of structure is accompanied by an evolution of function. The relatively simple and uniform metabolism of the undifferentiated blastodermic membranes gradually increases in complexity and variety, as the individual tissues and organs make their appearance and assume even a slight degree of functional activity. As to the periods at which different organs begin to functionate, but little is positively known.

The primitive heart, in all probability, begins to pulsate very early, as in an embryo from fifteen to eighteen days old and measuring but 2 mm. in length, Coste found the amnion, the allantois, the omphalo-mesenteric vessels, and the two primitive aortæ developed. In the earlier weeks, all products of metabolism are doubtless eliminated by the placental structures; but as metabolism increases in complexity the liver and kidney assume excretory activity. Thus, at the end of the third month the intestine contains a dark, greenish, viscid material—meconium—composed of bile pigments, bile salts, and desquamated epithelium; the amniotic fluid, as well as the fluid within the bladder, contains urea at the end of the sixth month, indicating the establishment of both hepatic and renal activity. Contractions of the skeletal muscles of the limbs begin about the fifth month, from which it may be inferred that the mechanism for muscle activity, viz.: muscles, efferent nerves, and spinal centers, has become anatomically developed and associated, and capable of coördinate activity. These contractions are, in all probability, automatic or autochthonic in character due to stimuli arising within the spinal centers. The remaining organs remain more or less inactive.

After birth, with the first inspiration and the introduction of food into the alimentary canal, the physiologic mechanisms which subserve general metabolism begin to functionate and in the course of a week are fully established. At this time the cardiac pulsation averages about 135 a minute; the respiratory movements vary from 30 to 35 a minute, and are diaphragmatic in type; the urine, which was at first scanty, is now abundant and proportional to the food consumed; the digestive glands are elaborating their respective enzymes, digestion proceeding as in the adult. The hepatic secretion is active and the lower bowel is emptied of its contents; the coördinate activites of the nerve-, muscle-, and gland-mechanisms are entirely reflex in character. Psychic activities are in abeyance by reason of the incomplete development of the cerebral mechanisms.

APPENDIX

PHYSIOLOGIC APPARATUS

The study of the physical and physiologic properties of muscles and nerves necessitates the employment of some stimulus which, when applied to either tissue, will call forth a contraction of the muscle, or the development of a nerve impulse in the nerve. The most convenient stimulus is electricity, for the reason that, with appropriate apparatus, its intensity and duration can be graduated with the utmost nicety. Moreover, it does not destroy the tissues, as do many chemic, physical, and mechanic stimuli.

It is, therefore, necessary that the student should have a practical acquaintance with those appliances by means of which electricity is generated, applied and controlled.

The **electric cell** is an apparatus composed of different elements, which, by virtue of chemic actions taking place among them, generate and conduct electricity. In its simplest form an electric cell consists of two metals—zinc and copper, or carbon, or platinum, etc., immersed in an exciting fluid, usually dilute sulphuric acid (Fig. 335).

The zinc element is the one acted on chemically by the sulphuric acid, and at the expense of which the electricity is maintained. It is known as the *generating* element. The copper is the *collecting* and *conducting* element.

With the immersion of these elements in a solution of H_2SO_4 a chemic action at once takes place between the zinc and the acid, with the formation of zinc sulphate and the liberation of hydrogen, as expressed in the following formula:

$$Zn + H_2SO_4 = ZnSO_4 + H_2.$$

The zinc sulphate passes into the solution, while the hydrogen accumulates on the surface of the copper element.

As all chemic action is accompanied by the development of electricity, it can be shown by appropriate means that this is the case at the surface of the zinc. Such a combination is the means of establishing *a difference of potential between two points*; the point of highest potential being in the acid at the surface of the zinc, the point of lowest potential being in the interior of the zinc. So long as the elements remain unconnected there is no movement of electricity, no current.

If the ends of the elements projecting beyond the fluid are connected by a copper wire, a pathway or circuit is established, and a movement of the electricity takes place. As electricity flows from the point of high to the point of low potential, it follows that inside the cell the current flows in the acid from the zinc to the copper, and outside the cell from the copper to the zinc. Such a current is termed *a continuous, a galvanic* or *a voltaic current.* Inasmuch as there is a progressive fall in potential between the highest and lowest points, it follows that any two points in the circuit will exhibit a similar difference of potential. For this reason the projecting end of the copper element is at a higher potential than the projecting end of the zinc element. The end of the copper is, therefore, termed the positive, + pole or *anode*, the end of the zinc the negative, − pole or *kathode*.

Electric Units.—Owing to the difference of the electric potential in the cell, the electricity leaves the cell under a certain degree of pressure, termed the "electro-motive force." As it passes through the circuit it meets with resistance, the amount of which will depend on the nature of the circuit material, its length, and the area of its cross-section. In accordance with the resistance will depend the quantity of electricity that a given electromotive force will press through in a unit of time. The strength of the current will, therefore, not depend entirely on the electro-motive force, but rather on the ratio between the electro-motive force and the resistance.

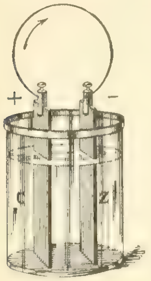

FIG. 335.—AN ELECTRIC CELL.

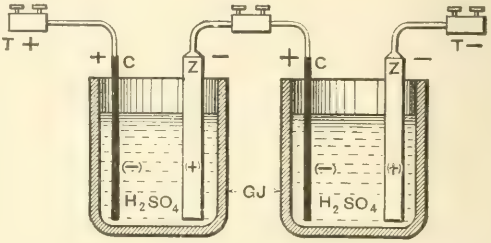

FIG. 336.—TWO SIMPLE ELECTRIC CELLS JOINED IN SERIES. C. Copper. Z. Zinc.

For the measurement of electric quantities, a system of units has been devised. The unit of electro-motive force is the volt; the unit of resistance is the ohm, *i.e.*, the resistance offered by a column of mercury 106.3 cm. long and 1 sq. mm. section at 0°C.; the unit of quantity is the coulomb; the unit of time is one second. One volt is the electro-motive force which, when steadily applied, will press through a resistance of the ohm, one coulomb of electricity in one second of time yielding a current strength of one ampere.

The relation may be expressed in the following formula, Ohm's law:

$$\text{C (current strength)} = \frac{\text{Electro-motive force (E. M. F.)}}{\text{Resistance (R)}} \text{ or Ampers} = \frac{\text{Volts}}{\text{Ohms}}$$

In practical work it is often necessary to increase the strength of the current. This is done by uniting two or more cells in series, *i.e.*, uniting the copper of one cell to the zinc of a second, and so on (Fig. 336). If the resistance remains the same the total voltage and current are those of one cell multiplied by the number of cells united.

The cell as above described cannot maintain a current of constant strength for any length of time, for the following reasons:

1. The sulphuric acid solution, in consequence of its chemic action, soon becomes nothing more than a saturated solution of zinc sulphate, after which its chemic activity ceases. The current, therefore, soon diminishes in strength.

2. The accumulation of hydrogen bubbles on the surface of the copper hinders the passage of the electricity. In a short time they develop a current in the opposite direction, which also tends to weaken the original current. This action is termed polarization of the elements.

Cells of this character are not suited for physiologic work, in which constancy in the strength of the current is absolutely necessary. To overcome these disadvantages, cells have been devised which are less violent in action, which prevent polarization, and which maintain a current of constant strength for a long period of time. One of the most generally used for physiologic purposes is—

The Daniell cell.—This consists of a porous cup containing a saturated solution of $CuSO_4$, copper sulphate, in which is immersed a copper plate or rod. This combination is placed in a glass vessel containing a solution of H_2SO_4 (1:15). In this solution is immersed a roll of sheet zinc (Fig. 337). Each of the plates is provided with a binding screw. When the cell is in action the sulphuric acid attacks the zinc, forming zinc sulphate, and liberates hydrogen; the cup being porous, the hydrogen passes into the copper sulphate solution, where it combines with the sulphuric acid radicle, and liberates metallic copper. Polarization of the copper is thus prevented. The metallic copper is deposited on the copper plate, which is thus kept bright. The copper sulphate solution is kept at the point of saturation by packing around the copper cylinder a quantity of the crystals of the salt. The sulphuric acid passes back into the porous cup, to take the place of that used. This cell is remarkably constant for these reasons, and well adapted for physiologic as well as other purposes where a current of uniform strength is necessary.

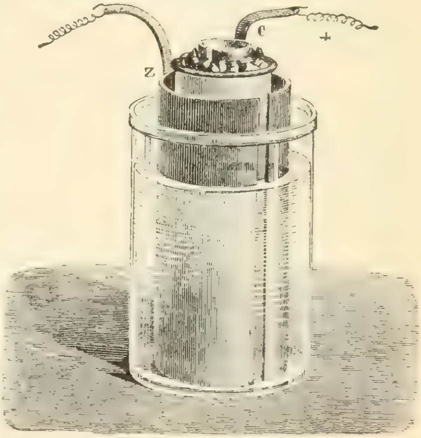

FIG. 337.—DANIELL CELL.

The projecting ends of the copper and zinc plates are termed respectively the positive pole or anode, and the negative pole or kathode. The electromotive force of a Daniell cell is practically 1 volt; but when the two poles are connected by a wire of 1 ohm resistance, the current strength will be less than 1 ampere, possibly only 0.7, owing to the resistance offered to the flow of electricity by the fluids between the zinc and the copper. In all measurements, the internal resistance of the cell must be taken into consideration.

The Dry Cell.—The commercial dry cell is a convenient source of electricity for general laboratory work. It consists of a cup of zinc, the inner surface of which is covered over with a thick layer of a paste of plaster of Paris, saturated with ammonium chlorid. In the center of the cup there is a rod of carbon. Surrounding this rod and occupying the space between it and the plaster-of-Paris paste, is a mixture of manganese dioxid and charcoal. The upper surface of the cell is sealed to prevent evaporation. The electricity is generated at the surface of the zinc cup by the chemic action of the chlorin which arises from the dissociation of the ammonium chlorid. When the plates are united by a conjunctive wire the current within the cell flows from the zinc (the positive element) to the carbon (the negative element), and without the cell from the carbon (the positive pole) to the zinc (the negative pole).

Leads.—By means of insulated wires attached to the poles of a cell, the electricity may be conducted from the cell and used for exciting or stimulating purpose. As the wires thus become practically prolongations of the plates their ends become the corresponding poles. In experimental work the ends of the wires are provided with special devices, termed—

Non-polarizable Electrodes.—The necessity for the employment of such electrodes arises from the fact that when the ends of the wires from a cell are placed in direct contact with the tissues chemic changes are produced in a short time, which lead to their polarization. As a result, a current opposite in direction to that of the cell is developed, which tends to weaken or neutralize it. This polarization current vitiates the result of many experiments made with highly irritable tissue such as nerve-tissue. Whether for stimulating purposes or for the purpose of detecting the existence of electric currents in living tissues, it is essential that the electrodes used shall be non-polarizable. The earliest electrodes of this character were made by du Bois-Reymond and were based on the fact discovered by Regnault that a strip of chemically pure zinc or amalgamated zinc (Matteucci) immersed in a saturated solution of zinc sulphate would not polarize. One form made by du Bois-Reymond is shown in Fig. 338. It consists of a flattened glass tube attached to a universal joint and supported by an insulated brass stand. The lower end of the tube is closed with kaolin or China clay made into a paste with a 0.6 per cent. solution of sodium chlorid. It can be moulded into any desired shape. The interior of the tube is partially filled with a saturated solution of sulphate of zinc in which is immersed the strip of amalgamated zinc. To the upper end of the zinc the conducting wire is attached.

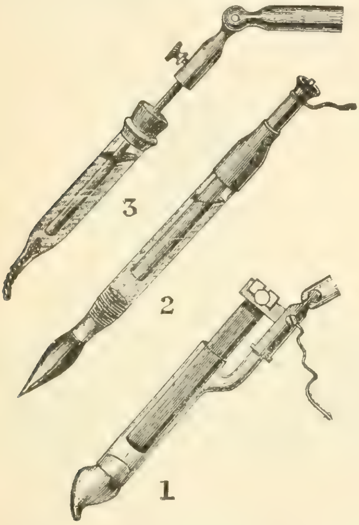

Fig. 338.—Non-polarizable Electrodes. 1. Du Bois-Reymond's. 2. Von Fleischl's. 3. d'Arsonval's.

The v. Fleischl brush electrode is similar to the preceding except that the end of the tube is closed by the brush of a camel's-hair pencil.

The d'Arsonval electrode consists of a glass tube containing a silver rod coated with fused silver chlorid. The interior of the tube is filled with normal salt solution 0.6 per cent. and the end closed with a thread or plug of asbestos which is made to project beyond the tube for a short distance.

Any one of these three electrodes is suitable for physiologic experimentation, as their free ends neither corrode the tissues nor develop electric currents.

Keys.—Muscle and nerve-tissues are conductors of electricity. When, therefore, the terminals (the non-polarizable electrodes) of the wires of a cell are placed in contact with either a muscle or a nerve a circuit is *made* through which a current of electricity flows; when one or both are removed, the circuit is *broken* and the current ceases. In practical work it is often necessary to keep the electrodes in contact with the tissues for a variable length of time. The circuit, however, may be alternately *made* and *broken* at will by interposing along the return wire a mechanic contrivance known as a key, of which there are many forms.

The du Bois-Reymond Friction Key.—This consists of a plate of vulcanite attached to a screw clamp by which it can be fastened to the edge of a table (Fig. 339). The surface of the vulcanite plate carries two rectangular blocks of brass, each of which has two holes drilled through it, for the insertion of wires, which are held in position by small screws. A movable bridge of brass, provided with an ebonite handle, serves to make connection between the blocks. There are two ways of interposing this key in the circuit.

1. *As a Simple Key.*—For this purpose one of the wires, usually the negative, is carried from the cell to one block and then continued from the second block. When the bridge is down, the circuit is made and the current passes; when it is up, the circuit is broken.
2. *As a Short-circuiting Key.*—When used for this purpose, the wires of the cell are carried to the inner holes of each block and then continued from the outer holes to the tissues or to some form of apparatus which it is desired to actuate. When the key is closed, *i.e.*, when the bridge is down, the current on reaching the key, will divide, one portion passing across the bridge and so back to the cell, the other portion passing to the tissue or apparatus. The amount of the current which is returned to the cell through the short circuit will be proportional to the resistance of the longer circuit. As the latter is usually great in comparison with the former, practically all the current is short-circuited. When the bridge is lowered, therefore, the current is short-circuited; when it is raised, the current flows into the longer circuit through the tissue or apparatus.

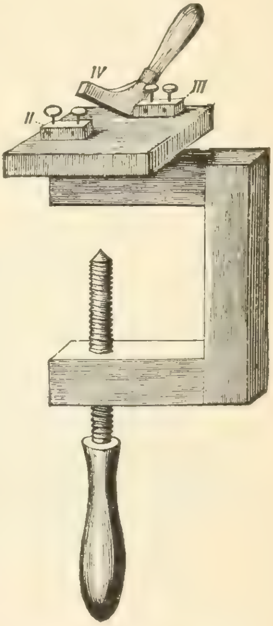

Fig. 330.—Du Bois-Reymond Friction Key.

The Mercury Key.—In this form the connection is established by means of mercury. It consists of a circular block in the center of which there is a cup containing mercury (Fig. 340). At opposite points there are binding posts, one of which is provided with a rigid fixed copper rod passing into the mercury; the other is provided with a movable bent rod which may be made to dip into or be withdrawn from the mercury by the ebonite handle.

The effect of a constant or galvanic current on a muscle or nerve will depend to some extent on its strength. This may be accurately regulated by means of an apparatus known as—

The Rheocord.—With this apparatus an electric current may be divided, one portion continuing through a conductor back to the battery, the other portion being sent off through the nerve. The strengths of these two currents are inversely proportional to the resistances of their circuits. A simple form of rheocord (Fig. 341) consists of a long wire arranged for convenience in parallel lines on a small wooden base and connected at its two ends with binding posts A and B. The resistance of this wire, 1.6 ohms, can be increased by the introduction of small resistance coils, between D and B, varying from 5 to 20 ohms.

The two binding posts A and B are connected with the positive and negative poles of an electric cell respectively. A simple key is placed in the circuit.

From A, a wire passes to one of the electrodes on which the muscle or nerve rests. A second wire passes from the second electrode to a clamp S, by way of the binding post C, which can be fastened to the long wire at any given point. The current, on reaching A, will divide into two branches, one of which will pass along the wire A, B, and thence back to the cell; the other will pass through the nerve and back to S and thence also to the cell. The amount of current passing through the nerve circuit will be inversely proportional to the resistance of the nerve and directly proportional to the difference of potential between A and S. If S is close to A, the difference of potential is slight. If S is removed from A toward B, the difference of potential is increased and the current sent through the nerve circuit is increased.

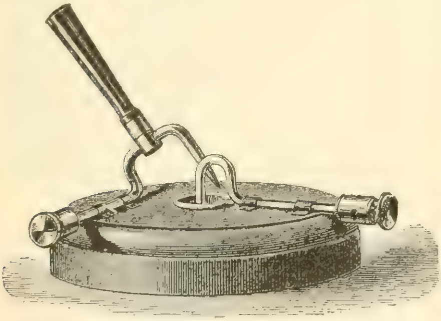

FIG. 340.—A MERCURY KEY.

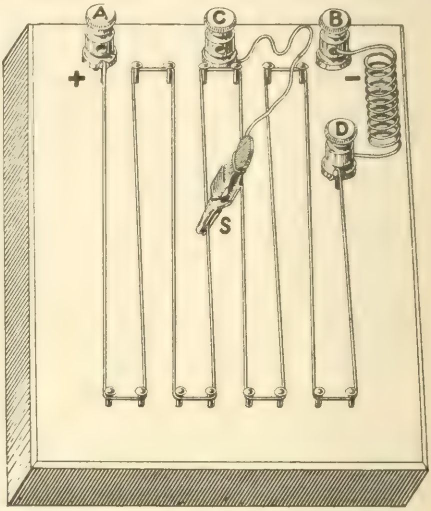

FIG. 341.—RHEOCORD.

In many experiments it is necessary to *reverse* the direction of the current, in other experiments to *deflect* it, without changing the position of the electrodes. Both these results may be accomplished by the use of—

Pohl's commutator. This is a round block of wood with six cups, each of which is in connection with a binding post (Fig. 342). In each of the two cups marked 1 and 2, + and −, is inserted one end of a copper wire bent at right angles. The other ends of the wires are supported and insulated by a hard-rubber handle. To the top of each wire is soldered a semicircular copper wire. This arrangement permits of a rocking movement, whereby the opposite ends of the semicircular wires can be made to dip into cups 3 and 4, and into cups 5 and 6 alternately. Two wires crossed in the middle of the block serve to connect opposite pairs of cups. When in use, the cups are filled with clean mercury. The method of using the commutator is as follows:

1. *As a Current Reverser.*—The positive and negative poles of the electric cell are connected by wires with binding posts 1 and 2 respectively. A key is interposed in the circuit. Wires are then carried from binding posts 3 and 4 to the electrodes in connection with the muscle or nerve. The rocker of the commutator is so turned that the ends of the semicircular wires dip into cups 3 and 4. The direction of the current will be on the closure of the circuit from 1 to 3, then from 3 along a wire to and through the tissue and back to 4, and thence to the cell. If the position of the rocker be now reversed so that the opposite ends of the semicircular wires dip into cups 5 and 6, the direction of the current through the tissue will be reversed. The positive current, after entering binding post 1, will flow to 5; then along one of the cross wires to 4; then along a wire to and through the tissue and back to 3, along the opposite cross wire to 6, thence to 2 and so back to the cell.

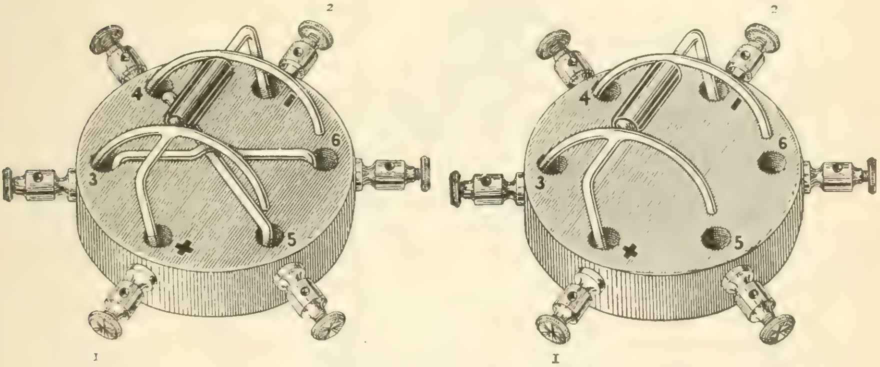

FIG. 342.—POHL'S COMMUTATOR. A. Arranged as a current reverser; B, as a current deflector.

2. *As a Current Deflector.*—When it is desirable to deflect the current to two pairs of electrodes differently situated, wires are carried from binding posts 3 and 4 to one pair, and from 5 and 6 to the other pair. The cross wires are then removed. According to the position of the rocker the current will be deflected to one or the other.

The Inductorium.—This is an apparatus designed for the purpose of obtaining single or rapidly succeeding electric currents by induction. Its construction is based on facts discovered by Faraday, some of which are the following:

If two circuits, a *primary* and a *secondary*, are placed parallel to each other, the former connected with a galvanic cell, the latter with a galvanometer, it is found that, at the moment the primary circuit is made, and at the moment it is broken, a current is *induced* in the secondary circuit, as shown by a momentary deflection of the galvanometer needle. During the continuous flow of the current through the primary circuit there is no evidence of a current in the secondary circuit. The induced current is but of momentary duration. The current flowing through the primary circuit is termed the *inducing*, the current flowing through the secondary circuit the *induced* current.

The induced current is *opposite* in direction to that of the inducing current when the circuit is made or closed; it is the *same* direction, however, when the circuit is broken or opened.

If the circuits are arranged in the form of coils, it is found that, other things being equal, the strength of the induced currents will be proportional to the number of turns in the coils.

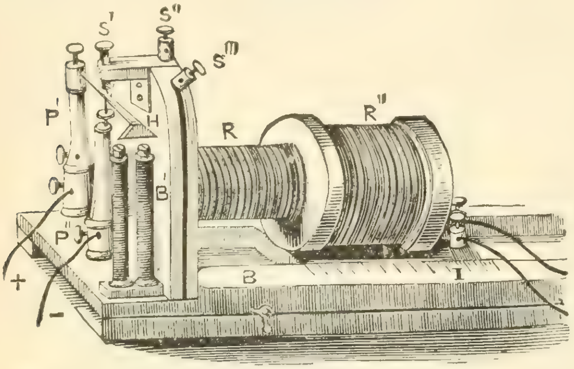

Fig. 343.—Inductorium of du Bois-Reymond. R′, Primary, R″ secondary spiral. B. Board on which R″ moves. 1. Scale. + —. Wires from battery. P′, P″. Pillars. H. Neef's hammer. B′. Electro-magnet. S′. Binding screw touching the steel spring (H). S″ and S‴. Binding screws to which to attach wires where Neef's hammer is not required.

If the coils are placed at varying distances from each other, the strength of the induced current varies, *increasing* as the coils are approximated, *decreasing* as they are separated.

Approximation or separation of the coils while the current is flowing through the primary circuit develops an induced current, which disappears, however, the moment the movement of the coil ceases. A sudden increase or decrease in the strength of the inducing current also develops an induced current.

When the coils are approximated or the primary current increased in strength, the induced current is opposite in direction to that of the inducing current; with the reverse conditions, the induced current has the same direction.

The *induced currents* have been termed, in honor of their discoverer, Faradic currents.

The **du Bois-Reymond inductorium,** based on the foregoing facts, consists essentially of two coils of insulted copper wire, termed primary and secondary (Fig. 343).

The primary coil, R′, consists of thick copper wire wound around a wooden spool attached to a vertical support. The beginning of this coil is at the binding post S″, its termination either at binding post P″ or S‴. In the course of this primary wire or circuit, there are placed two vertical bars of soft iron, B′, connected at their bases to form a horseshoe magnet, around the ends of which the wire is coiled. The object of this device will be explained later.

Inside the primary coil there is placed a bundle of soft iron wires, which, as soon as the circuit is made, become magnetized, with the effect of increasing the action of the inducing current.

The secondary coil, R″, consists of a much greater number of turns of a finer copper wire, the ratio being about 40 to 1, also wound around a spool, having a tunnel sufficiently large to enable it to slide over the primary. By these means the strength of the induced current is increased. As a result of the construction of the inductorium, the low electro-motive force of the cell is transformed into the high electro-motive force characteristic of the induced current. As the number of turns of wire in the secondary coil is to the number in the primary, so are the electro-motive forces in the secondary coil to those in the primary coil.

The secondary coil slides along a track, B, which permits it to be moved toward or away from the primary. The distance between the two coils can be measured and the strength of the induced current again reproduced, other things being equal, by means of a centimeter-millimeter scale pasted on the edge of B.

The ends of the wire of the secondary coil are fastened to two binding posts to which conducting wires provided with hand electrodes can be attacked.

The inductorium may be used for obtaining either a single current or a series of rapidly repeated induced currents.

The Single Induced Current.—On account of its high electro-motive force, its penetrative power, and short duration, the single induced current is a most convenient and suitable form of stimulus for many purposes. In order to obtain such a current, the positive wire of the cell is carried to binding post S″, and the negative wire either to S‴ or P″. A key is placed in the primary circuit. The course of the current will then be on the closure of the circuit from the cell to S″, thence around R′ to S‴, and so back to the cell; or if the negative wire is connected with P″, the course of the current on leaving R′ will be through the coils surrounding the two vertical bars B′, thence to P″, and so back to the cell. If the secondary coil be placed close to the primary and the wires of the secondary brought into contact with a muscle, it will be found that with both the make and the break of the primary circuit a current is induced in the secondary, as shown by a short quick pulsation of the muscle; but during the time of closure of the circuit the induced current is wanting, as shown by the quiescent condition of the muscle. It will be apparent, however, from the energy of the contraction that the break-induced current is a more efficient stimulus than the make-induced current. That this is the case is made evident by removing the secondary to the end of the slide-way and then gradually bringing it toward the primary half a centimeter at a time, making and breaking the circuit after each movement until a pulsation of the muscle occurs. It will be found to occur first on the break of the circuit. As the secondary approaches the primary a position will be reached when a pulsation occurs on the make as well as on the break of the circuit, though it will be less pronounced.

The explanation offered for this difference in the strength of the two induced currents is as follows: With the make of the circuit and the passage of the battery current through the primary coil there is induced in the neighboring and parallel turns of the wire and *extra* current opposite in direction to the primary current. This extra or self-induced current antagonizes and prevents the current from attaining its maximum development as quickly as it otherwise would, and therefore its efficiency as an inducer of a current in the secondary is diminished. On the break of the circuit the primary current disappears quickly, and as there is nothing to retard its disappearance its efficiency as an inducer of a current in the secondary coil is not diminished. It is not infrequently stated that the disappearance of the primary current induces in the neighboring coils a *break-extra* *current* corresponding in direction which assists in the development of the induced current. This is not the case, however, as no break-extra current is developed in the inductorium as ordinarily used when actuated by a battery current of moderate strength.

As it is not so much the intensity of the current as it is rapid variations in intensity that produce effects, it is readily apparent why the induced current developed at the break of the primary is more effective as a stimulus than the induced current developed at the make of the primary circuit. The quantity of electricity is, however, the same in both cases.

If the secondary be pushed further along the slideway until it largely covers the primary coil, a position will be reached when the make-induced current equals in its efficiency as a stimulus the break-induced current; and if the secondary be yet further advanced, a position is reached when the make-induced current becomes more powerful and efficient than the break-induced current, as shown by the greater contraction of the muscle. This result is explained by the fact that the make-extra current is now able of itself to induce a current in the secondary coil, on account of its proximity, which, added to that induced by the battery current, produces a current, greater than that induced on the break of the circuit.[1]

Rapidly Repeated Induced Currents.—As the single-induced current is of extremely short duration, it is inefficient as a stimulus in the conduct of many experiments. It is necessary, therefore, to develop it with a frequency that is sufficient to give rise to a summation of effects. The duration of the stimulation may be thus considerably prolonged. This is accomplished by introducing in the primary circuit close to the primary coil an automatic interrupter, usually Neef's modification of Wagner's hammer (Fig. 344). This consists of a vertical post, P′, to the top of which is fastened a metallic spring carrying at its opposite end a steel or iron hammer, H, which hangs over, but does not touch, the two vertical bars of soft iron around which the wire of the primary coil is wound. About the middle of the spring on its upper surface there is a small plate of platinum which is in contact with an adjustable, platinum-tipped screw, S′, carried by a plate of brass in connection with binding post S″.

For the purpose of interrupting the primary circuit frequently in a unit of time, and thus developing induced currents in quick succession, the apparatus is arranged in the following way: The positive and negative poles of the electric cell are connected by wires with binding post P′ and P″, a key being interposed in the circuit. If the screw S′ is in contact with the spring, the current on the closure of the circuit will enter P′, pass along the spring to S′, thence into and through the primary coil R′, to the coils surrounding the vertical bars B′, then to P″, and so back to the cell.

As the current passes around the vertical bars, they are magnetized. The magnetization draws down the hammer, and, in so doing, breaks the circuit at the tip of the screw, S′. The vertical bars are at once demagnetized, and the hammer is restored to its original position by the elasticity of the spring. The circuit is thus reëstablished, the current flows through the coils, the bars are again magnetized, the hammer is drawn down, to be followed by a second break of the circuit.

The number of times the circuit is thus *made* and *broken* per second will vary with the length of the spring.

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[1] "On certain peculiarities of the inductorium," Prof. Colin C. Stewart, "Univ. Pa. Medical Bulletin," Feb., 1904.

As each interruption of the primary circuit develops an induced current, it follows that the latter must succeed each other with a frequency corresponding with the frequency of the former. If while the primary circuit is thus being interrupted the wires of the secondary coil be placed in contact with a muscle, the induced current will give rise to contractions which will succeed each other so rapidly that they fuse together, producing a spasm or *tetanus* of the muscle. For this reason these currents are frequently spoken of as *tetanizing* currents, and the procedure as *tetanization* or *Faradization*. These currents also increase in strength as the secondary approaches the primary.

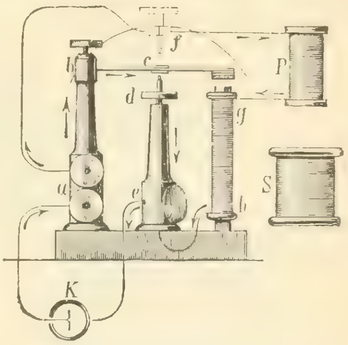

FIG. 344.—HELMHOLTZ'S MODIFICATION OF NEEF'S HAMMER. As long as *c* is not in contact with *d*, *g h* remains magnetic; thus *c* is attracted to *d* and a secondary circuit, *a*, *b*, *c*, *d*, *e*, is formed; *c* then springs back again, and thus the process goes on. A new wire is introduced to connect *a* with *f*. K. Battery.

Helmholtz's Modification of the Inductorium.—With a view of equalizing the strengths of the induced currents, Helmholtz suggested a device the adoption of which accomplishes this to a certain extent. It consists (Fig. 362) in connecting with a wire binding posts P′ and S″, and in providing binding post P″ with an adjustable screw which can be raised until the spring comes in contact with it, when the hammer is drawn down by the electromagnet B′. This latter arrangement is practically a short-circuiting key by which a portion of the current is returned to the cell without ever entering the primary coil. The same arrangement, though differently lettered, is shown in Fig. 363. By the use of the entire device the changes in the primary coil are made not by making and breaking the primary current, but by alternately long- and short-circuiting the current. "When the short-circuiting key is opened, the full volume of the primary current flows through the primary coil. When the short-circuiting key is closed, most of the current fails to enter the coil, taking the easier path through the key. Some of the current, however, always flows through the coil and is never diverted. The cycle of changes in the electric condition of the primary coil is thus altered for two reasons:

"First, we no longer have an alternation between a full primary current and none at all—rather an alternation between a full primary current and a weaker one. The difference in the phases is thus lessened, the extent of the change on making and breaking is lessened, and correspondingly the efficiency of the make and break currents induced in the secondary coil is slightly decreased.

"Second, on making the primary current, as in the ordinary coil, the sudden appearance of the primary current is antagonized by the opposing make-extra current, with the result that the make-induced current is still further reduced; while on breaking the current the break-extra current can now flow through the primary coil across the short-circuiting key. This current, trailing behind the disappearing primary current in the same direction, produces the same effect as if the primary current itself were to disappear slowly. As a result the disappearance of the primary current loses its former efficiency as an inducer of secondary currents, and the break-induction current is reduced to about the efficiency of the make.

"This so-called 'equalizing' of the make- and break-induced currents is never perfect, if for no other reason, because the make-extra current must take the long circuit through the battery, while the break-extra current has an easier path through the short-circuiting key, and is thus greater than the make-extra current." (C. C. Stewart.)

THE GRAPHIC METHOD

The term graphic is applied to a method by which curves or tracings are obtained which represent the extent, duration, and time relations of the movements accompanying physiologic processes. If these movements can be translated in one direction, they may be recorded in different ways:

1. By attaching the moving structure—*e.g.*, heart, muscle, etc.—to a

delicate lever the free extremity of which is provided with a writing point.

2. By transmitting the movement through a column of air enclosed in a rubber tube the two ends of which are attached to a metallic capsule, covered by a rubber membrane, termed a drum or tambour. When the membrane of the first tambour is pressed or driven inward, the air is forced through the rubber tube into the second tambour and its membrane is pushed outward. As soon as the primary pressure is removed, the membranes return to their former condition. If the membrane of the first tambour is drawn outward, the air in the system is rarefied and the membrane of the second tambour is pressed inward. For the purpose of registering the movement transmitted by the column of air, the second tambour is provided with a light lever supported by a vertical bearing resting on a small metallic disc. The membrane of the first tambour is frequently provided with a button, which is placed over the moving structure. The inward movement of the membrane of the first tambour produces an outward movement of the membrane of the second tambour, indicated, though magnified, by the rise of the free end of the lever. The reverse movement of the membrane is attended by a fall of the lever. The first tambour is termed the *receiving*, the second the *recording* tambour (Figs. 345, 346).

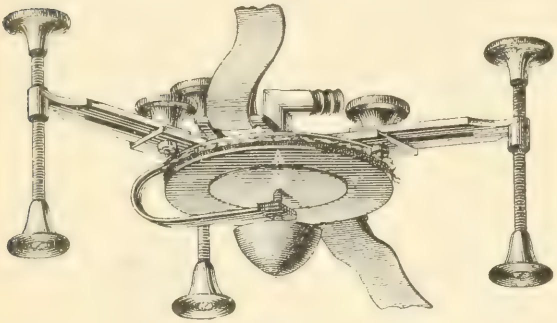

FIG. 345.—A RECEIVING TAMBOUR.

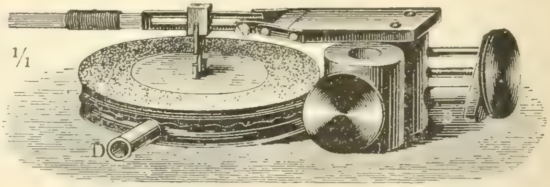

FIG. 346.—A RECORDING TAMBOUR.—(*Marey.*)

3. By enclosing an organ—*e.g.*, kidney, spleen, arm, finger, etc.—in a rigid glass or metal vessel which at one point is in communication with a recording apparatus—*e.g.*, (1) a piston provided with a lever (page 467); or (2) a tambour and lever (page 357); or (3) a mercurial manometer carrying a float and pen (page 343). The space between the part investigated and the vessel is filled with fluid. The variations in volume of the organ cause a displacement of the fluid and give rise to a to-and-fro movement which is taken up and reproduced by the recording apparatus.

The writing point may be (1) some form of pen carrying ink which records the movement on a white paper surface, or (2) a piece of metal, glass, or paper which records the movement on smoked paper or glass.

The Recording Surface.—The surface which receives and records the movements of a pen or lever is usually that of a cylinder which is covered with glazed paper and coated with a thin layer of soot, obtained by passing the cylinder through the flame of a gas burner. The axis of the cylinder is supported by a metal framework. If the writing point of the lever be placed against the cylinder and a movement be imparted to it, a portion of the soot is rubbed off, leaving a white line behind. If the cylinder be stationary, the rise and fall of the lever are recorded as a vertical line. Such a record shows only the extent of a movement. If the cylinder is traveling, however, at a uniform rate, the rise and fall of the lever are recorded in the form of a curve the width of the two arms of which will depend partly on the rapidity of the movement of the lever and partly on the rate of movement of the cylinder. The cylinder movement is initiated and maintained by clock-work or by the transmission of power by belting to a system of pulleys in connection with its axis. As the tracing is wave-like in form, the cylinder is frequently spoken of as a kymograph or wave recorder (Fig. 347).

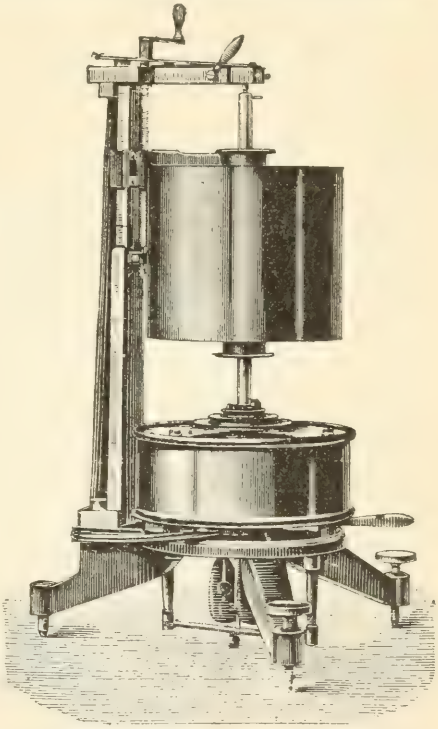
FIG. 347.—KYMOGRAPH. (Boruttau's, Petzold, Leipzig.)

From the record thus obtained it is possible to determine not only the extent but also the duration, the form, and the rate of recurrence of any given movement.

The Extent of a Movement.—As the lever not only takes up and reproduces a movement, but at the same time magnifies it, it is essential that the degree of magnification be known, in order to determine the actual extent of the movement. The magnification of the lever is readily determined by dividing the distance between the axis of the lever and its writing point by the distance between the axis and the point of attachment of the structure, and then dividing the height of the tracing by this quotient. The final quotient represents the extent of the movement.

The Time Relations of a Movement.—When recorded in the form of a curve, the duration of the entire movement, or of any one portion of it, can be determined by means of a time marking or chronographic apparatus, consisting of (1) a small signal magnet provided with a movable armature, to which is attached a writing style; (2) an automatic interrupter; and (3) an electric cell.

The Signal Magnet.—The magnet (Fig. 348) is actuated by the electric current made and broken at regular and known intervals by an automatically acting interrupter placed in the circuit. With each make and break of the circuit the armature and style move alternately downward and upward. The excursion of the style can be readily recorded on a traveling surface. The character and number of the interruptions per second will determine the character of the tracing. If they occur in a rhythmic manner, the tracing will be sinusoidal or wave-like in form. If the time of interruption is of short duration as compared with the time of closure of the circuit, the tracing will be a horizontal line with short vertical elevations at regular intervals.

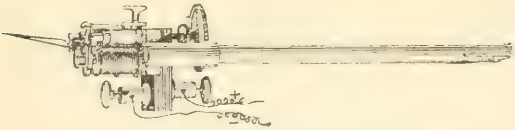

FIG. 348.—SIGNAL MAGNET.

The Automatic Interrupter.—The circuit may be interrupted by vibrating reeds, tuning-forks, metronomes, etc. A well-known form of vibrating reed is shown in Fig. 349. This consists of a metallic frame carrying a coil of wire in the center of which there is a core of soft iron. To the vertical part of the frame there is fastened the reed, the distal end of which is bent to dip into an adjustable mercury cup. When in circuit the current enters the coil, then flows into and through the frame and the reed to the mercury, and thence back to the cell. On the closure of the circuit and the magnetization of the iron core the reed is withdrawn from the mercury, the circuit broken, and the core demagnetized. The elasticity of the spring returns it to the mercury, when the circuit is again restored. The reed may be so constructed that it will be raised and lowered 50, 100, or 200 times a second. The armature of the signal magnet undergoes a corresponding number of elevations and depressions. If the reed vibrates 100 times in a second, the distance from crest to crest of the wave tracing will represent $\frac{1}{100}$ of a second. Interrupters of various kinds have been devised which make and break the circuit from 1 to 250 times a second.

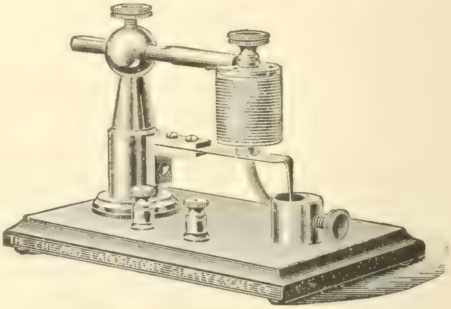

FIG. 349.—PAGE'S VIBRATING REED. (Reichert's modification.)

Moist Chamber.—In many experiments, it is necessary to keep the nerve or muscle preparation in a uniformly moist atmosphere. To secure this, a moist chamber is employed (Fig. 350). This consists of a hard-rubber platform, supported by a piece of brass, which slides up and down a vertical rod, and which can be clamped at any height. By means of a short lever the vertical rod can be turned, carrying the platform from side to side. The rod is secured to a firm iron base.

Six double binding posts for the attachment of wires pass through the platform. Near the side of the upper surface of the platform there rises a vertical rod, carrying a clamp for holding the femur of a nerve-muscle preparation, as well as a horizontal rod for supporting at least three pairs of non-polarizable electrodes. A groove around the outer edge of the platform receives a glass shade, which covers the whole. The air of the chamber is kept moist by placing in it pieces of blotting-paper saturated with water.

From the under surface of the platform there descends a rod, which, by means of a double binding screw, supports a horizontal rod, modified at one end to carry the delicate axis of a light stiff recording lever. The end of this lever is pointed, to enable it to write on a smoked glass or paper. Beneath the axis is a strip of brass, carrying a screw, which gives support to the lever until the instant the contraction of the muscle begins. This screw, the after-loading screw, also enables the lever to be placed in a horizontal position. The portion of the lever near the axis is provided with a double hook, the lower portion of which serves for the attachment of the weight by which the muscle is counterpoised.

In some experiments, as in the registration of a muscle contraction under varying conditions, it is necessary to give the lever mass by attaching weights directly beneath the muscle. This, however, introduces certain errors in the movements of the lever, which somewhat deform what would otherwise be the normal curve. If the weight be attached, not opposite to the muscle attachment, but close to the axis of the lever, the undesirable acceleration of the lever movement, during both contraction and relaxation, is largely prevented. The lever may be a straw, a strip of celluloid or aluminium. It should be as light as possible. The writing point may be made of stiff paper, a piece of tinsel, glass, or aluminium. It should have sufficient elasticity to keep it in contact with the cylinder during the excursion of the lever. The writing point should be placed as nearly parallel as possible to the surface of the cylinder.

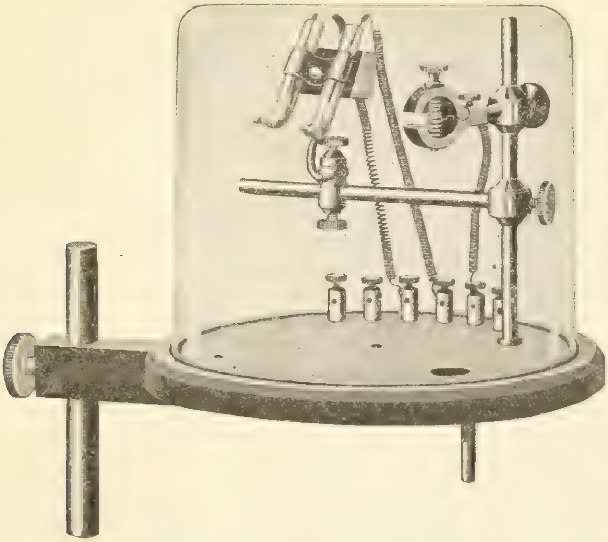
FIG. 350.—MOIST CHAMBER.

Normal Saline Solution.—To prevent drying and a loss of irritability the tissue under investigation should be kept moist with the normal saline solution (NaCl, 0.6 per cent.). This solution very largely prevents either absorption or extraction of water from the tissues and thus retards chemic changes in their composition.

Ringer's solution, largely used for the same purpose, is made by saturating 0.65 per cent. NaCl solution with calcium phosphate and then adding 2 c.c. of a 1 per cent. solution of potassium chlorid to each 100 c.c.

The Galvanometer and Capillary Electrometer.—In the detection and investigation of the electric currents of muscles, nerves, and other tissues, the physiologist is limited to the galvanometer and capillary electrometer. The principle of the galvanometer is based on the fact that an electric current flowing through a wire parallel in direction with a magnetic needle will tend to set the needle at right angles to the direction of the current. The essential requisite of any galvanometer used for physiologic purposes is that it will respond quickly to the influence of extremely weak currents. This is realized by the use of small light needles, the adoption of the astatic system, or some similar device by which the directive influence of the earth's magnetism is eliminated, and the multiplication of the number of turns of the wire in the coils which surround the needle.

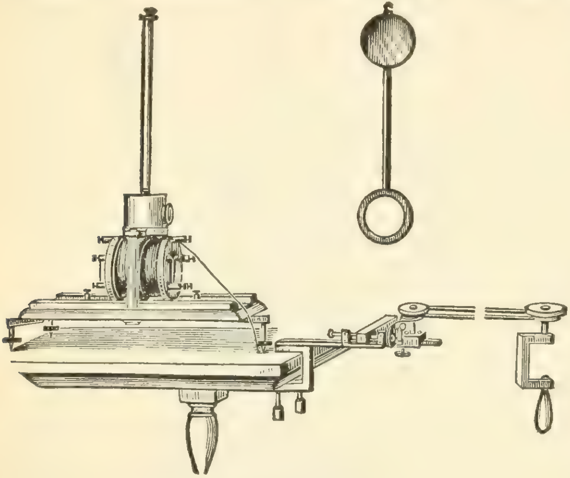
FIG. 351.—WIEDEMANN'S BOUSSOLE.

The tangent galvanometer, or *boussole,* as constructed by Wiedemann, is the form most frequently employed in physiologic investigations (Fig. 351). It consists primarily of a thick copper cylinder, through which a tunnel has been bored. Within this tunnel is suspended a magnetized ring, just large enough to swing clear of the sides of the chamber. The object of making the magnet ring-shaped is to increase its strength in proportion to its size, and to get rid of the central inactive part. Connected with and passing upward from the magnetized ring through the copper cylinder is an aluminium rod, surmounted by a circular plane mirror. Above the mirror rises a glass tube, which carries on top, on an ebonite support, a little windlass, capable of being centered by three small screws. On the windlass is wound a single filament of silk, which passes down the tube and is attached to the mirror. The magnet can, by this contrivance, be raised or lowered and centered in the copper chamber. Deflections of the mirror from currents of air are prevented by inclosing it with a brass cover provided with a glass window. The coils are placed on each side of the copper chamber, and supported by a rod, on which they slide. By this arrangement they can be approximated until they meet and completely conceal the cylinder. By varying the position of the coils the influence of the current upon the needle can be increased or diminished. An advantage which this galvanometer possesses is the damping of the oscillation of the needle, so that it quickly comes to rest after deflection. This is accomplished by the development of induction currents in the copper cylinder, the direction of which is opposite to that of the movement of the needle. The instrument, therefore, is aperiodic—that is to say, when the needle is influenced by a current it moves comparatively slowly until the maximum deflection is reached, when it comes to rest without oscillations. When the circuit is broken the needle swings slowly back to zero, and again comes to rest without oscillations.

Inasmuch as the needle is not astatic, it is rendered so by the use of an accessory magnet—the so-called Hauy's bar. This magnet, supported by a rod directed perpendicular to the coils, is placed in the magnetic meridian, horizontal to the needle, with its north pole pointing north. By sliding the magnet toward the needle the directive influence of the earth's magnetism is gradually diminished, and when it is reduced to a minimum the needle acquires its highest degree of instability. By means of a pulley an angular movement can be imparted to the end of the accessory magnet in the direction of the magnetic meridian, which serves to keep the needle on the zero of the scale. The deflections of the needle are observed by means of an astronomic telescope, above which is placed a scale divided into centimeters and millimeters, and distant from the galvanometer about six or eight feet. As the numbers on the scale are reversed, they will be seen in the mirror in their natural position, and with the deflection of the needle the number will appear as if drawn across the mirror. The extent of the deflection is readily determined when the needle comes to rest.

The reflecting galvanometer of Sir William Thompson is also used for the same purposes.

The Capillary Electrometer.—Not withstanding the extreme sensitiveness of the modern galvanometer, it has been found desirable, in the investigation of many physiologic processes, to possess some means which will respond even more promptly to slight variations in electro-motive force. This has been realized in the construction by Lippmann of the capillary electrometer. The principle of this apparatus rests upon the fact that the capillary constant or the surface-tension of mercury undergoes a change upon the passage of an electric current, in consequence of a polarization by hydrogen taking place at its surface. If a capillary glass tube be filled with mercury and its lower end inserted into a solution of sulphuric acid, and the former connected with the positive and the latter with the negative electrode, it will be observed, upon the passage of the current, that a definite movement of the mercury takes place, in the direction of the negative electrode, in consequence of the diminution of its capillary constant or the tension of its surface in contact with the acid. As a reverse movement follows a cessation of the current, a series of oscillations will follow a rapid making and breaking of the current. If the direction of the current is reversed, the capillary constant is increased and the mercury ascends the tube toward the negative pole. From facts such as these Lippmann constructed the capillary electrometer, a convenient modification of which devised by M. v. Frey, is shown in Fig. 352. This consists of a glass tube, *A*, forty millimeters in length, three millimeters in diameter, the lower end of which is drawn out to a fine capillary point. The tube is filled with mercury and its capillary point immersed in a 10 per cent. solution of sulphuric acid. The vessel containing the acid is filled to the extent of several millimeters with mercury also. The mercury in the tube is put in connection with a platinum wire (*a*), and the acid in the vessel with a second wire (*b*). When a constant current passes into the apparatus in the direction from *b* to *a* the mercury is pushed up the tube, and, upon the breaking of the current, it may or may not return to the zero-point. For the purpose of measuring in millimeters of mercury the pressure necessary to compensate this change in the capillary constant produced by the electro-motive force of polarization, the apparatus is provided with a pressure-vessel, *H*, and a manometer, *B*. This electrometer can be applied to any microscope having a reversible stage. The oscillations of the mercury can then be observed with the microscope provided with an ocular micrometer (Fig. 353). The special advantage of the electrometer is, that it will respond instantly to any variation in the electro-motive force and indicated a difference of potential, according to Lippmann's observation, as slight as the $\frac{1}{10080}$ of a Daniell. These rapid oscillations can be recorded by photographic methods.

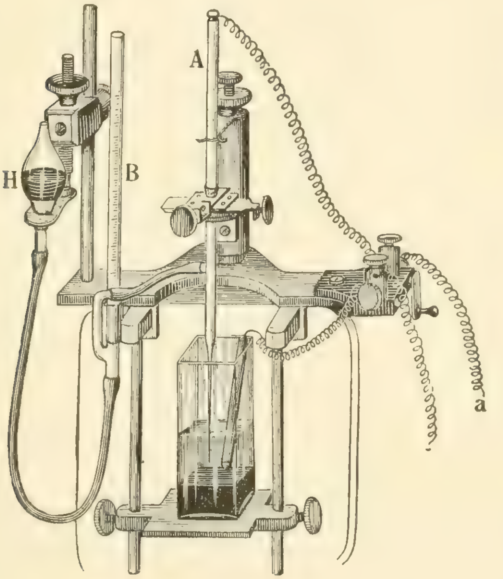

Fig. 352.—Von Frey's Capillary Electrometer.

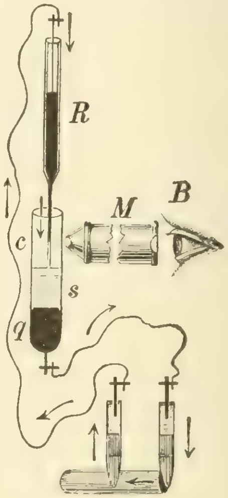

Fig. 353.—Capillary Electrometer. *R*. Mercury in tube; capillary tube. *s*. Sulphuric acid. *q*. Hg. *B*. Observer. *M*. Microscope.

In using either the galvanometer or the electrometer for detecting the existence of electric currents or differences of potential in living tissues, it is absolutely essential that non-polarizable electrodes be employed in connection with it.

The String Galvanometer.—The string galvanometer (Fig. 354) as devised by Einthoven is a far more sensitive apparatus than either the usual galvanometer or the capillary electrometer, and responds to feeble electric currents more quickly than either. It is based on the principle that a conductor placed near a stationary magnet will tend to change its position when a current is passed through it, just as a magnet, *e.g.*, a delicate magnetic needle, placed near a conductor will change its position when a current is passing through the conductor. For the purpose of developing a high degree of sensitiveness, two strong magnets are employed, across the field of which runs a very fine conductor usually made by drawing out molten quartz, by means of a bow and arrow, to a thread much thinner than the smallest possible metal wire, and then silvering the filament to enable it to conduct electricity. When the filament is securely fastened at its extremities, it will be found that it will deviate to the right or the left according to the direction of the current which enters it.

By reason of the small size of the filament employed, it must be strongly illuminated, and the shadow of the thread must be magnified by an optical device and then projected across a narrow slit on a sensitive surface behind it. As the shadow of the thread moves from side to side at the same time that the sensitive surface moves in a direction at right angles to it, a graphic record will be obtained in which the abscissa will indicate time and the ordinates, the displacement of the thread or the strength of the current passing through it. A typical normal record or electro-cardiogram (Fig. 133, page 292) shows three upward directed waves separated by two smaller downward directed waves and these are commonly designated, following Einthoven, by the letters P, Q, R, S, T in order. In the conduct of an experiment a patient's extremities are connected with some suitable low-resistance electrodes. Under such circumstances a part of the heart's action currents may be led off to the filament of the galvanometer. If the circuit is completed from the right arm and the left arm, the arrangement is called lead I; if from the right and left leg lead II; if from the left arm and the left leg, lead III.

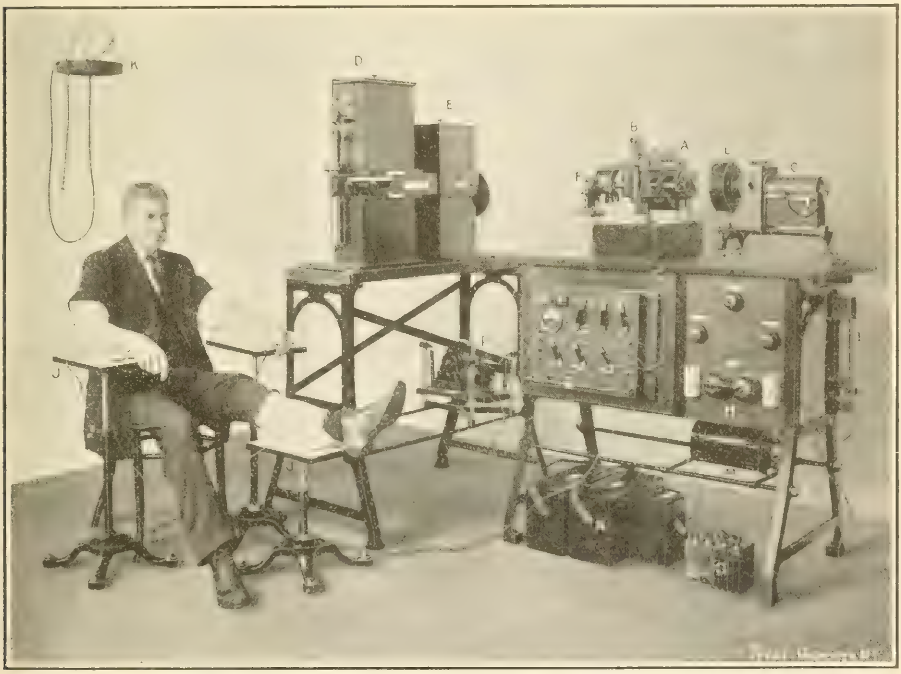

FIG. 354.—THE CAMBRIDGE ELECTRO-CARDIOGRAPH OR STRING GALVANOMETER.

The apparatus is customarily arranged so that the current produced by electro-negative auricles and electro-positive ventricles gives an upward loop to the tracing, one centimeter of height being made to correspond to an electro-motive force of one millivolt on suitable adjustment of the quartz filament.

Various forms of string galvanometers, based on the principle stated in a previous paragraph, have been devised. The apparatus shown in Fig. 354 is known as the Cambridge Electro-cardiograph.

DISSECTION OF THE HIND-LEG OF THE FROG

Much of our knowledge of the physiologic properties of muscles and nerves has been derived from the study of the muscles and nerves of the cold-blooded animals, especially of the frog, for the reason that in these animals the tissues retain their vitality under appropriate conditions for a considerable period of time after death or removal from the body. The muscles generally employed for experimental purposes are the gastrocnemius, the sartorius, the semimembranosus, the gracilis, and the hyoglossus. The nerve generally employed is the sciatic. Both muscle and nerve may be studied independently of each other, or they may be studied together, as when in their usual physiologic relation. For this latter purpose the gastrocnemius muscle and sciatic nerve are employed, constituting the so-called "nerve-muscle preparation."

For these, and many other reasons, the student should familiarize himself with the general anatomy of the frog, and especially with the anatomy of the posterior extremities.

Preparation of the Frog.—Destroy the frog by plunging a pin through the skin and soft tissues covering the space between the occipital bone and the first vertebra until the point is stopped by the vertebra. Turn the pin toward the head and push it into the brain cavity; move it from side to side and destroy the brain. Pass the pin into the spinal canal and destroy the spinal cord. With a stout pair of scissors cut off the body behind the fore limbs. Remove the viscera and the abdominal walls. Draw the hind-legs out of the skin. Place the legs on a glass plate, back uppermost, and moisten them freely with normal saline solution.

Observe on the outer side of the dorsal surface of the thigh the following muscles (Fig. 355, 356). The triceps femoris (tr), made up of the rectus anticus (ra), the vastus externus (ve), and the vastus internus (vi), not seen from behind; on the inner side, the semi-membranosus (sm) and the rectus internus minor or gracilis (ri″). Between these two groups, note the biceps femoris (b). Above the thigh observe the gluteus (gl), the ileo-coccygeus (ci), and the pyriformis (p).

In the leg observe the gastrocnemius (g) with its tendon (the tendo-Achillis), the tibialis anticus (ta), and the peroneus (pe).

Turn the frog on its back and note the muscles on the ventral surface of the thigh, the rectus internus major (ri′), and minor (ri″), the adductor magnus (ad″), the sartorius (s), the adductor longus (ad′), and the vastus internus (vi). In the leg, in addition to those already seen from behind, note the tibialis posticus (tp) and the extensor cruris (ec).

Note in the abdominal cavity the three large spinal nerves, the seventh, eighth, and ninth.

Dissection of the Sciatic Nerve.—The sciatic nerve is composed of the seventh, eighth, and ninth spinal nerves. After its emergence from the pelvic cavity, it passes down the thigh between the semi-membranosus and the biceps muscles, in company with the femoral blood-vessels. Below the knee it divides into the tibialis and peroneus nerves; the former sending branches into the gastrocnemius. In its course, the sciatic sends branches to the muscles of the entire leg.

Carefully separate the biceps and semimembranosus by tearing the connective tissue uniting them. The sciatic nerve and femoral blood-vessels come into view; with a bent glass rod gently separate the nerve from its surroundings from the knee to the thigh. Begin at the knee. In order to expose the nerve at the pelvis, it will be necessary to divide the pyriformis and the ileo-coccygeus muscles. Care must here be exercised, so as not to injure the nerve which lies immediately beneath. Lift up the urostyle with the forceps and separate it from the last vertebra. With the scissors cut off the vertebral column above the seventh vertebra. Place the legs on the dorsal surface and then divide the seventh, eighth, and ninth vertebræ lengthwise. With the forceps lift up one lateral half of the vertebræ and free the nerve as far as the knee by dividing connective tissue and nerve branches. Be careful not to injure the nerve with scissors or forceps.

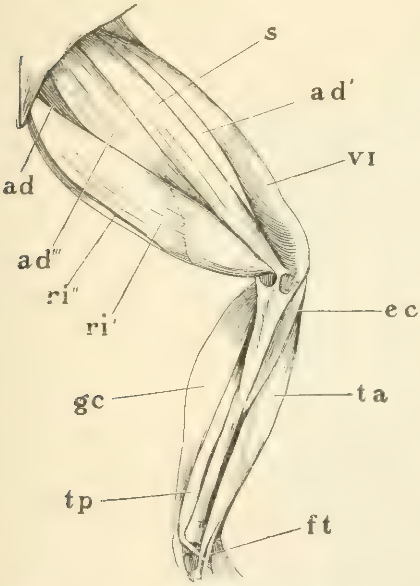

FIG. 355.—LEG MUSCLES OF THE FROG. VENTRAL SURFACE.—(*Ecker.*)

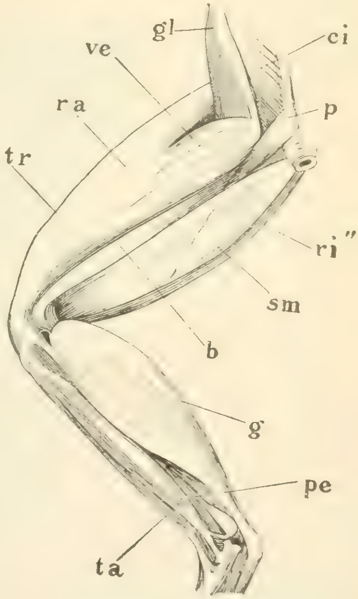

FIG. 356.—LEG MUSCLES OF THE FROG. DORSAL SURFACE.—(*Ecker.*)

The Nerve-muscle Preparation.—Divide the tendo-Achillis just below its fibro-cartilaginous thickening at the heel, and detach the gastrocnemius up to the knee. Cut through the tibio-fibular bone just below the knee-joint. Cut the femur transversely near its middle and remove the muscles from the lower end, carefully avoiding injury to the nerve. The completed preparation consists of the gastrocnemius muscle, the sciatic nerve, with half of the seventh, eighth, and ninth vertebræ and the lower half of the femur.

THE ANATOMY OF THE FROG HEART AND THE VASCULAR APPARATUS

The heart of the frog can be readily exposed after the animal has been made insensible by destruction of the brain. The sternum is divided longitudinally and each half drawn outward by gentle traction of the anterior extremities. The pericardium is then divided and turned aside.

When viewed from the ventral surface, Fig. 375, the heart shows two auricles, a right and left, a single ventricle and a more or less conical vessel, the *conus arteriosus*, which arises from the right side of the base of the ventricle. When viewed from the dorsal surface, Fig. 376, it presents a triangular-shaped vessel, the *sinus venosus*, formed by the union of the terminations of the two superior and inferior venæ cavæ. A dissection of the heart shows that the cavity of the sinus venosus communicates with the cavity of the right auricle by means of a transversely oval foramen, in the posterior wall of the auricle. This opening is provided with two valves, a ventral and dorsal, the free edges of which are directed toward the cavity of the auricle. Two pulmonary veins, a right and left, penetrate the dorsal wall of the left auricle.

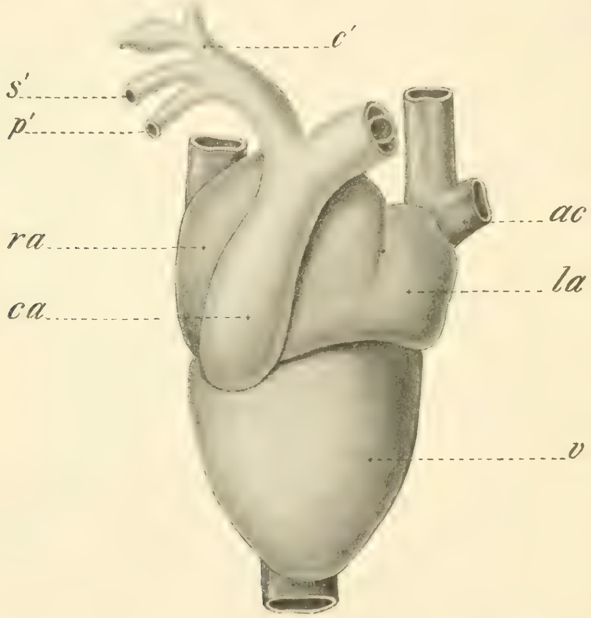

FIG. 357.—VENTRAL SURFACE OF THE FROG HEART. (*After Howes.*) *ra*. Right auricle *la*. Left auricle. *v*. Ventricle. *ca*. Conus arteriosus. *p′*. Pulmo-cutaneous trunk. *s′*. Systemic aortic trunk. *c′*. Carotid trunk. *ac*. Left anterior caval vein.

A longitudinal section, Fig. 377, of the heart shows that the auricles, though separated by a septum, communicate below by a common orifice with the cavity of the single ventricle. This orifice, the auriculo-ventricular, is provided with two valves the free edges of which are directed toward the cavity of the ventricle.

The conus arteriosus is separated from the ventricle by three semilunar valves. The interior of the conus is traversed by a longitudinally disposed membranous valve attached to its dorsal surface; the ventral edge is, however, free. The upper extremity of the conus passes into the *bulbus aortæ*, from which it is separated by a semilunar valve and the free extremity of the longitudinal valve. From the bulbus aortæ arise two large branches, a right and a left, each of which is subdivided by two longitudinal partitions into three vessels, the carotid trunk, the aortic arch, and the pulmo-cutaneous trunk. (See Fig. 377.) The carotid and aortic trunks communicate separately with the cavity of the bulbus, while the pulmo-cutaneous trunk communicates with the conus arteriosus by a single orifice, just below the free end of the longitudinal valve. After pursuing a short course these three vessels separate from one another to distribute blood to the various organs of the body. The two aortic trunks wind around the esophagus and unite posteriorly to form the dorsal aorta; the pulmo-cutaneous divides into a pulmonary artery which is distributed to the lung and a cutaneous branch which is distributed to the skin.

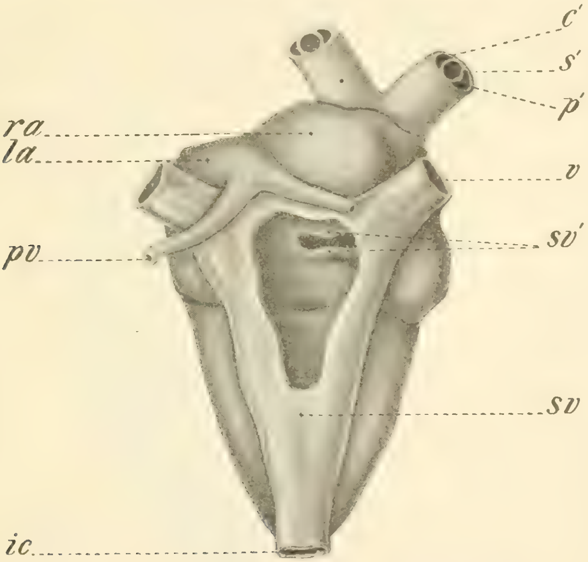

Fig. 358.—Dorsal Surface of the Frog Heart. (*After Howes.*) *ra.* Right auricle. *la.* Left auricle. *sv.* Sinus venosus. *sv′.* Opening of sinus venosus into right auricle. *pv.* Pulmonary vein. *v.* Right anterior caval vein. *p′ s′ c′.* The pulmo-cutaneous, aortic and carotid trunks respectively.

The course of the blood through the heart cavities is, therefore, as follows: The venous blood poured by the venæ cavæ into the sinus venosus passes through the sino-auricular foramen into the right auricle. While the right auricle is being filled from this source, the left auricle is being filled by blood coming through the pulmonary veins. "When the auricles contract, which they do simultaneously, each passes its blood into the corresponding part of the ventricle, which then instantly contracts before the venous and arterial bloods have time to mix. Since the conus arteriosus springs from the right side of the ventricle it will at first receive only venous blood, which on the contraction of the conus might pass either into the bulbus aortæ or into the aperture of the pulmo-cutaneous trunks. But the carotid and systemic trunks are connected with a much more extensive capillary system than the pulmo-cutaneous and the pressure in them is proportionally great, so that it is easier for the blood to enter the pulmo-cutaneous trunks than to force aside the valves between the conus and the bulbus. A fraction of a second is, however, enough to get up the pressure in the pulmonary and cutaneous arteries, and in the meantime the pressure in the arteries of the head, trunk, etc., is constantly diminishing, owing to the continual flow of blood toward the capillaries. Very soon, therefore, the blood forces the valves aside and makes its way into the bulbus aortæ. Here again the course taken is that of least resistance; owing to the presence of the carotid gland, the passage of blood into the carotid trunks is less free than into the wide elastic systemic trunks. These will, therefore, receive the next portion of blood which, the venous blood having been mostly driven to the lungs, will be a mixture of venous and arterial. Finally as the pressure rises in the systemic trunks the last portion of blood from the ventricle, which coming from the left side is arterial, will pass into the carotids and so supply the head" (Parker and Haswell).

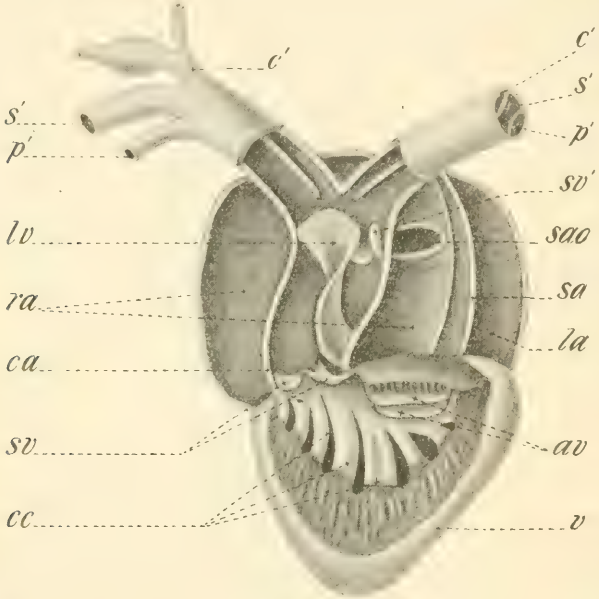

FIG. 359.—FROG HEART WITH VENTRAL SURFACE DISSECTED AWAY TO SHOW ITS STRUCTURE. (*After Parker and Haswell.*) *ra.* Right auricle. *la.* Left auricle. *sa.* Septum between auricles. *sao.* Sino-auricular opening. *ca.* Conus arteriosus. *sv.* Semilunar valves. *av.* Auriculo-ventricular valves. *lv.* Longitudinal valve. *sv′.* Semilunar valve. *p′ s′ c′.* Pulmo-cutaneous aortic and carotid trunks respectively. *cc.* Columnæ carneæ.

The muscle-fibers composing the walls of the heart from the sinus venosus to the conus arteriosus are continuous, though at the sino-auricular, the auriculo-ventricular, and the ventriculo-conic junctions the continuity is to some extent interrupted by bands of circularly disposed fibrous tissue, serving for the support of the valves, which momentarily interfere with the ready passage of the contraction wave from one division of the heart to another. The frog heart receives its nutritive material from the blood flowing through its cavities. During the diastole the blood, under the influence of the slight pressure developed, passes from the interior of the heart into a system of irregular passageways or channels which penetrate the heart-wall in all directions, and thus comes into direct contact with the heart-cells. With the beginning of the systole the blood is forced out of these channels into the interior of the ventricle, bringing with it the products of tissue metabolism.

The Heart-beat.—If the heart while beating is lifted up by a ligature attached to the apex it will be observed that the contraction begins in the walls of the sinus venosus, then passes to the auricles, thence to the ventricle and finally to the conus; from this it may be inferred that the physiologic stimulus acts primarily in the walls of the sinus from which its effect, viz.: the excitation process, is conducted from one cavity to another in quick succession.

INDEX

Abducent nerve, 626
Aberration, chromatic, 702
    spheric, 702
Absorption, 210
    by epithelium of villi, 219
    of foods, 218
        of fat, 222
        of proteins, 220
        of sugar, 220
        of water, 220
    of lymph, 217
    spectra of blood, 248
A-C interval, 302
Acapnia, 431
Accommodation of the eye, 694
    convergence of eyes during, 698
    force of, 697
    mechanism of, 695
    range, 697
Acoustic or auditory area, 587
    nerve, 631
Action currents of muscles, 79
        of nerves, 106
    reflex, 114
        of medulla oblongata, 564
        of spinal cord, 537, 541
Adams-Stokes syndrome, 304
Adrenal bodies, 500
Agraphia, 594
Albuminoids, 16
Albumins, 15
Alcohol, effects of, 126
Alimentary canal, 136
Amino-acids, 13
Amnion, 734
Amylase, 152
Amylogenesis, 487
Amylopsin, 191
Amyloses, 7
Anastalsis, 201
Animal body, structure of, 2
Animal heat, 438
Ankle clonus, 543
    jerk, 543
Anti-dromic vaso-dilatator nerves, 380
Aphasia, 594
    agraphic, 594
Aphasia, amnesic, 595
    aphemic, 594
Apnea, 433
    chemica or vera, 434
    vagi or inhibitoria, 434
Arterial circulation, 328
    pressure, 343
Arteries, structure and properties of, 328
Articulate speech, 593
Articulation, temporo-maxillary, 143
Asphyxia, 435
Association centers of cerebrum, 596
Astigmatism, 701
As-Vs interval, 302
Auriculo-ventricular node, 272
Autonomic nerve system, 642
    anatomic relation of central nerve system to sympathetic ganglia, 647
    anatomic relation of, to peripheral structures, 644
    autonomic or sympathetic ganglia, 644
        autonomic nerves from mid-brain region, 647
            bulbar region, 647
            mid-spinal cord, 648
            sacral, 649
        functions of autonomic nerve system, 651
        functions of the mid-brain autonomic nerves, 651
            bulbar, 652
            sacral autonomic, 654
            thoracic and lumbar, 652

Basal ganglia, 557
Bile, 195
    composition of, 195
    mode of secretion, 197
    physiologic action, 198
    pigments, 197
    salts, 195
Bilirubin, 197
Biliverdin, 197
Bioplasm, 29
    physiologic properties, 29
Blind spot, 704

Blood, 230
    changes in, during respiration, 412
    circulation of, 264
    coagulation of, 234
        chemistry of, 261
        extravascular, 262
        intravascular, 263
    constituents of, 230
    corpuscles, 238, 252
    defibrinated, 235
    general composition of, 269
    physical constitution, 230
    physical properties of, 231
    plates, 259
    pressure, 341
        arterial, 343
        capillary, 347
        causes of, 340
        determination of, in man, 355
        methods of estimation, 346
        auscultatory method, 358
        résumé of factors, 348
        variations in, 350
        venous, 347
    quantity of, 260
    reaction, 232
    serum, 236
    temperature, 233
    velocity of, in arteries, 360
        of, in capillaries, 362
        of, in veins, 363
        viscosity of, 233
Bronchial innervation, 390
Burdach, column of, 533

Calcium salts of the body, 20
Calorimeter, 444
Capillary blood-vessels, 330
        functions of, 331
    circulation, 371
    electrometer, 757
Capsule, internal, 560
    functions of, 567
Carbo-hemoglobin, 251
Carbohydrates, 7
Carbon monoxid hemoglobin, 251
Cardiac cycle, 275
    impulse, 274
    movement of the blood during, 277
    schematic representation of the events, 288
Cardiac nerves, 313
Cardio-accelerator center, 322
    factors which determine its activity, 323
Cardio-inhibitor center, 323
    factors which determine its activity, 324
Cardio-pulmonic vessels, 267
Carotid pulse, 368
Caseinogen, 16, 19
Catalysis, 139
Caudate nucleus, 558
Cells, structure of, 24
    chemic composition, 25
    manifestations of life by, 26
    reproduction of, 28
Central organs of the nerve system, 523
Cerebellar tract, 533
Cerebellum, 603
    functions of, 605
    results of experimental lesions, 605
Cerebrum, 570
    convolutions of, 572
    fissures of, 570
    functions of, 577
    localization of function in, 578
    motor area of the chimpanzee brain, 584
    motor area of the human brain, 590
    motor area of the monkey's brain, 580
    sensor areas of the human brain, 585
    sensor areas of the monkey's brain, 581
    structure of the gray matter, 570
    structure of the white matter, 575
Chemic composition of the body, 6
Cheyne-Stokes respiration, 435
Chimpanzee brain, motor area of, 584
Cholesterin, 196
Chorda tympani nerve, 153, 630
Chorion, 735
Chromo-proteins, 17
Chyle, 223
Ciliary ganglion, 646
    movement, 88
    muscle, 682
        function of, 696
Circulation of blood, 264
    forces concerned, 375
    hydrodynamic considerations, 332
    vascular apparatus, 328
Clark's vesicular column, 530
Classification of food principles, 122
Coagulated proteins, 18
Cochlea, 718
    functions of, 723
Colostrum, 483
Color perception, 709
Commutator, 747

Complemental air, 407
Conjugated proteins, 17
Connective tissues, 33
    physical and physiologic properties of, 37
Coördination, mechanism of, 607
Coronary arteries, 295
    effects of ligation, 297
    vaso-motor nerves of, 296
Corpora quadrigemina, 556
        functions of, 565
    striatum, 557
        functions of, 566
Corpus luteum, 729
Cranial nerves, 610
Crura cerebri, 555
    functions of, 565
Crystalline lens, 685

Defecation, 207
    nerve mechanism of, 207
Degeneration, Wallerian, 99
Deglutition, 159
    nerve mechanism of, 164
Demarcation current, 80
Depressor nerve, 325, 386
Dextrin, 8
Dextroses, 8
Diabetes, 521
Diapedesis of leucocytes, 257
Diaphragm, 393–398
Diastalsis, 201
Diffusion, 225
Digestion, 136
Digestive apparatus, 136
Dilatator pupillæ muscle, 681
Direct cerebellar tract, 533
    pyramidal tract, 532
Ductless glands, 480
Ductus arteriosus, 739
    venosus, 739
Dyspnea, 434

Electro-cardiogram, 292
Electro-cardiograph, 759
Electrodes, non-polarizable, 744
Electrometer capillary, 757
Electrotonic alterations in excitability of nerves, 108
    current, 107
Electrotonus, 107
Encephalo-spinal fluid, 524
Endocardium, 266
Enterokinase, 194
Enzymes, 138
Epidermis, 492
Epididymis, 693
Epinephrin, 503
Epithelial tissues, functions of, 31, 32
Erepsin, 192, 193
Erlanger's sphygmomanometer, 356
Erythrocytes, 238
Eupnea, 433
Eustachian tube, 713, 722
Excretion, 453
Expiratory forces and muscles, 400
Expired air, composition of, 410
Eye, cardinal points of, 688
    blind spot, 704
    dioptric apparatus of, 686
    muscles of, 709
    physiologic anatomy of, 679
    reduced, 690
    schematic, 689

Facial nerve, 626
        function of, 628
        paralysis of, 627
Fallopian tube, 728
Fat, 11
    absorption of, 222
    digestion of, 192
    emulsification of, 12
    saponification of, 11
Feces, 206
Fecundation, 732
Fehling's solution, 8
Ferments, 138
Fetal circulation, 737
    membranes, 734
Fibrillary contraction, 297
Fibrin, 19
Fibrinogen, 237
Fillet, 544, 553
Filtration, 229
Follicle, Graafian, 726
Food, 116
    animal, 131
    cereal, 133
    composition of, 131
    disposition of, 123
    heat value of, 126
    principles, 122
    quantities required daily, 121
    vegetable, 134
Forced expiration, 401
Forces aiding the movement of lymph and chyle, 223
Fovea, 685
Frog heart, anatomy of, 762

Galactose, 9
Gall-bladder, 194
Galvanic current, effect of, on nerves, 107
    muscles, 59, 60, 81
Galvanometer, 756, 758
Ganglia, peripheral, 646
Gaseous exchange in lungs, 420
    in tissues, 420
Gases of blood, relation of, 413
        tension of, 417
    carbon dioxid, 416
    nitrogen, 417
    oxygen, 415
Gastric digestion, 165
    fistulæ, 169
    glands, 167
    juice, 170
        mode of secretion, 172
        physiologic action of, 174
Globulins, 15
Glossopharyngeal nerve, 633
Gluco-proteins, 17
Glycogen, 8, 487
    in muscles, 515
Glycogenesis, 487
Glycogenic function of the liver, 487
Glycogenolysis, 487
Glycolysis, 488
Glycosuria, 518
    alimentary, 518
    adrenal, 518
    pancreatic, 518
    parathyroid, 521
    pharmacologic, 520
    phlorhizin, 520
    pituitary, 520
Gmelin's test for bile pigments, 197
Goll, column of, 533
Gower's antero-lateral tract, 532
Graafian follicle, 726
Graphic method, 756
Green vegetables, 135

Hairs, 474
Hearing, sense of, 713
Heart, 264
    action of sympathetic nerve on, 313, 319
        of vagus nerve on, 317, 320
    auriculo-ventricular bundle, 271
    conduction system of, 302
    beat, nature of the stimulus, 305
        action of inorganic salts, 306
        cardio-pulmonic vessels, 267
        frequency of, 290
Heart beat, influence of psychic states, 325
        theory of, 308
        of the excised heart, 297
    blood-supply, 292
    causes of the variations of, 290
    compensatory pause, 310
    coronary arteries, 295
        effects of ligation, 297
        time of filling, 295
        vaso-motor fibers for, 296
    course of blood through, 267
    curve of the systole and diastole, 277
    cycle of 275
    extra-systole, 310
    idio-ventricular rhythm, 303
    intra-auricular pressure, 286
    intracardiac nerve-cells, 313
    intraventricular pressure, 282, 339
        curve, 276, 285
        distribution of, 341
    mechanics of, 273
    modifications of beat due to the action of drugs, 326
    muscle-band of His, 271
    muscle-fibers of, 269
    negative pressure of, 282
    nerve, mechanism of, 311
    orifices and valves, 268
    origin and distribution of the sympathetic nerves to, 311
    origin and distribution of the vagus nerve to, 314
    physiologic anatomy of, 264
    refractory period, 310
    relative function of auricles and ventricles, 280
    sounds, 279
    synchronism of the two sides, 281
    valves, action of, 278
    ventricular systole, 285
        the pre-sphygmic period, 286
        the post-sphygmic period, 286
        the sphygmic period, 286
    work done by, 376
Heart-muscle, properties of, 298
    automaticity, 305
    conductivity, 299
    electric currents of, 290
    electro-cardiograms, 292
    irritability, 298
    response to the action of an artificial stimulus, 309
    rhythmicity, 304
    tonicity, 305
Heat dissipation, 448

Heat, mechanism of, 447
    production, 441
    influence of the nerve system, 450
    relation to work, 437
    rigor, 65
Helmholtz's theory of color perception, 711
Hematin, 252
Hemianopsia, 588, 616
Hemoglobin, 244
    absorption spectra of, 249
    chemic composition of, 245
    quantity of, 245
Hemoglobinometer, Gowers', 246
    Haldane's, 247
Hemometer, v. Fleischl's, 248
Hering's theory of color perception, 711
Histons, 14
Hormone, 174
Horopter, 707
Hypermetropia, 700
Hyperpnea, 433
Hypoglossal nerve, 640

Ileo-colic sphincter, 203
Incus, 715
Indol, 205
Induced currents, 713, 749, 750
Inductorium, 747
Infra-proteins, 18
Insalivation, 146
    nerve mechanism of, 153
Inspiration, 397
    mechanic movements of thorax, 394
    muscles, 397
Insula, 574
Intercostal muscles, 393
Internal capsule, 560
        functions of, 567
    secretion, 490
Intestinal digestion, 185
    fermentation, 205
    juice, 193
        physiologic action of, 193
    movements, 200
    nerve mechanism of, 202
    rhythmic segmentation, 200
Intraauricular pressure, 286
Intracranial circulation, 597
    mechanism of, 598
Intrapulmonic pressure, 395, 402
Intrathoracic pressure, 395, 403
Intravascular coagulation, 263
Intraventricular pressure, 282
    distribution of, 341
Invertase, 194
Iris, 681
    functions of, 698
    nerve mechanism of, 619, 620
Iron of the body, 22
Irritability of muscles, 57
    of nerves, 101
Island of Langerhans, 188
    of Reil, 574
Isometric myogram, 69
Isotonic myogram, 64
Isthmus of encephalon, 553
    functions of, 564

Jacobson's nerve, 633, 634
Joints, 48
    classification of, 48

Katastalsis, 201
Keith-Flack node, 272
Kidney, 458
    histology of, 459
Knee-jerk, 542
Kymograph, 753

Labyrinth of ear, 715
Lacrimal glands, 712
Lactation, 481, 739
Lacteals, 223
Lactose, 10
Language, 592
Large intestine, 203
    function of, 204
    movements of, 204
    nerve mechanism of, 205
Larynx, 658
    nerve mechanism of, 666
    structure of, 659
Lateral columns of the spinal cord, 532
Law of contraction, 110
Lecithin, 197
Lemniscus, 544, 553
Lens, crystalline, 685
Lenticular nucleus, 558
Leucocytosis, 257
Leucopenia, 257
Leukocytes, 255
    chemic composition of, 256
    functions of, 259
    number of, 256
    origin of, 258
    physiologic properties, 257
    varieties of, 258
Levers, 83
Levulose, 9
Limbic lobe, 573

Liver, 194, 483
  conjugation of the products of protein putrefaction, 489
  elaboration of bile by, 486
  formation of urea in, 488
  functions of, 485
  influence of the nerve system on, 516
  production of glycogen and sugar, 487
Localization of functions in cerebrum, 578
Lungs, structure of the, 389
Lymph, 213
  absorption of, 217
  composition of, 215
  functions of, 217
  movement of, 223
  physical properties, 214
  production of, 215
Lymph-capillaries, 211
Lymph-glands, 212
Lymph-nodes, 212
Lymph-vessels, 212
Lymphocytes, 213, 258

Macula lutea, 684
Malleus, 715
Maltose, 10
Mammary glands, 479
Mastication, 141
  muscles of, 143
  nerve mechanism of, 144
Meats, composition of, 131
Medulla oblongata, 551
  reflex activities of, 564
Meibomian glands, 712
Membrana tympani, 714
  function of, 720
Menstruation, 729
Metabolism, 118, 509
  during starvation, 128, 510
  of carbohydrates, 515
  of fats, 513
  of proteins, 512
  on a mixed diet, 511
  on protein diet, 130
  on fat and carbohydrate diet, 131
Methemoglobin, 252
Migration of leukocytes, 257, 373
Milk, 480
  composition of, 132, 480
  mechanism of secretion, 481
Moist chamber, 755
Motor area of chimpanzee brain, 584
    of human brain, 585
    of monkey brain, 580
  oculi nerve, 617
Mouth digestion, 141
Movements of the eyeball, 708
  of the intestines, 200, 204
  of the lower jaw, 143
  of the lungs, 402
  of the stomach, 179
Muscle, action currents of, 81
  contraction, 63
    chemic phenomena of, 76
    electric phenomena of, 79
    graphic representation of, 63
    modifying influences of, 65
    phenomena following stimulation, 61
    physical phenomena of, 61
    rigor mortis, 76
    summation effects, 71
    tetanus, 72, 74
    thermic phenomena of, 78
Muscles, electric currents from, 79
  electric currents, negative variation of, 81
  energy, source of, 77
  fatigue, 68
  groups, special action of, 83
  sense, 674
  sound, 76
  spindle, 674
  stimuli, 59
  tissue, 51
    chemic composition of, 54
    elasticity, 56, 62
    histology of, 52, 85
    irritability, 57
    physical properties of, 55
    physiologic properties of, 55
    tonicity, 57
Myenteric plexus, 169, 202
  reflex, 202
Myopia, 700
Myosinogen, 15, 55
Myxedema, 490

Nerve, abducent, 626
  acoustic, 531
  facial, 626
  glosso-pharyngeal, 635
  hypoglossal, 640
  oculo-motor, 617
  olfactory, 612
  optic, 613
  pneumogastric, vagus, 634
  spinal accessory, 639
  trigeminal, 623
  trochlear, 622

Nerve impulse, 102
Nerve mechanism of heart, 311
        of respiration, 424
        of vascular apparatus, 376
Nerve-muscle preparation, 104, 761
Nerve system, functions of, 524
Nerve tissue, 90
    histology of, 90
Nerves, autonomic system of, 642
    chemic composition and metabolism of, 94
    classification of, 99
    degeneration of, 98
    development of, 97
    effects of galvanic current on, 107
    electric currents of, 104
    electric currents of, negative variation of, 105
    electric excitation of, 107
    electric phenomena of, 104
        action currents, 106
        diphasic action currents, 107
    peripheral endings of, 96
    physiologic properties of, 101
    pilo-motor, 100
    polar stimulation of, 110
    relation of, to central nerve system, 95
    stimuli of, 101
Neuron, 90
Nicotin, actions of, 158, 326
Nucleo-proteins, 17
Nucleus caudatus, 558
    cuneatus, 533
    gracilis, 533
    lenticularis, 558
Nutritive supply of the embryo, 736

Oculo-motor nerve, 617
Ohm's law, 742
Olein, 11
Olfactory nerve, 612
Oncometer, 467
Ophthalmic ganglion, 646
Opsonins, 259
Optic constants, 686
    nerve, 613
    thalamus, 558
        functions of, 566
Optogram, 706
Organ of Corti, 718
Osazones, 10
Osmometer, 227
Osmosis, 226
Osmotic pressure, 226
Ossicles of ear, 714
Otic ganglion, 647
Ovary, 726
Ovulation, 728
Ovum, 727
Oxygen in blood, 415
    in tissues, 418
    quantity absorbed daily, 410, 422
Oxyhemoglobin, 250

Pacinian corpuscle, 671
Palmitin, 11
Pancreas, 185
Pancreatic juice, 188
    mode of secretion, 189
    physiologic action of, 190
Parathyroids, 494
    effects of removal, 494
Partial pressure of gases, 414
Parturition, 738
Pepsin, 171
Peptones, 175
Peripheral organs of the nerve system, 523
Peristalsis, 158, 201
Peristaltic rush, 201
Perspiration, 471
Petrosal nerves, 629
Pettenkofer-Voit respiration apparatus, 421
Pexin, 171
Phagocytosis, 259
Phlorhizin glycosuria, 520
Phonation, 658
    mechanism of, 664
Phospho-proteins, 16
Physiology of the cell, 24
    of movement, 39
Pilleus ventriculi, 201
Pilo-motor nerves, 100
Pituitary body, 495
    effects of total removal, 496
        of anterior lobe removal, 497
        of injection of extracts, 499
        of posterior lobe removal, 498
Placenta, 736
Plasma of blood, composition of, 235
Pleura, 394
Pneumatogram, 406
Pneumogastric nerve, 634
Pneumograph, 406
Polar stimulation, 110
    of human nerves, 111
Pons varolii, 553
    functions of, 565
Postures, 84
Presbyopia, 699

Prosecretin, 190
Protamins, 14
Proteins, 12
    chemic composition, 12
    color reactions, 19
    physical properties, 13
    precipitation tests, 20
    structure of, 13
Ptyalin, 152
Pulmonic blood-vessels, 374, 391
    vascular apparatus, 374
    ventilation, 394
Pulse, 364
    carotid, 368
    frequency, 260, 367
    radial 366
    venous, 369
    volume, 290
    wave, velocity of, 366
Punctum proximum, 697
    remotum, 697
Pyramidal tracts of spinal cord, 532

Reaction of degeneration, 114
Red corpuscles, 238
    chemic composition of, 244
    effects of reagents, 243
    function of, 255
    life history of, 252
    number of, 240
    of vertebrated animals, 254
    preservation of, 242
Reduced hemoglobin, 250
Reflex action, 114, 536
    laws of, 539
Refractory period of the heart, 310
Regnault's and Reisset's respiration apparatus, 422
Relation of gases in the blood, 413
Renal duct, 462
Rennin, 171
Reproduction, 726
Reproductive organs of the female, 726
Reproductive organs of the male, 730
Reserve air, 407
Residual air, 398, 407
Residual heat of the body, 440
Respiration, 388
    changes in composition of air during, 409
    changes in composition of blood, 412
    changes in tissues, 418
    chemistry of, 409
    effects of a change of pressure of the blood gases on, 413
Respiration, expiratory forces and muscles, 400
    first inspiration, 432
    mechanism of gaseous exchange, 420
    nerve mechanism of, 424
    number per minute, 405
    total respiratory exchange, 421
    volumes of air breathed, 406
Respiratory apparatus, 388
    movements, 397
        effects of, on arterial pressure, 437
        effects of, on the flow of blood through the thoracic vessels, 436
        of upper air passages, 404
Respiratory nerve mechanism, 424
    inspiratory center, 425
        causes of rhythmic activity of, 425
        effect of a change of pressure of blood gases on, 431
        reflex stimulation, 427
        relation of vagus nerves, 427
        theories of mode of action, 430
Respiratory pressures, 395
    quotient, 411
    rhythm, 405
        Cheyne-Stokes, 435
        modification of, 433
    sounds, 409
    types, 405
Retina, 682
    functions of, 704
Retinal image, 686
        size of, 691
Rheocord, 746
Rhythmic segmentation, 200
Rigor mortis, 76
Rima glottidis, 658
    respiratoria, 625, 663
    vocalis, 663
Ringer-Locke solution, 307
Routes for the absorbed food, 223
Rush peristalsis, 201

Saccharose, 9
Saliva, 148
    physiologic action of, 150
Salivary glands, 146
        histologic changes in, during secretion, 150
        modification of by drugs, 157
        nerve mechanism of, 153
Sclero-proteins, 16
Sebaceous glands, 474
Sebum, 474
Secretin, 190

Secretion, external, 476
  internal, 490
Semen, 731
Semicircular canals, 716, 724
Sensor areas of human brain, 585
  of monkey brain, 581
Serum, 236
Setchenow's center, 541
Sight, sense of, 679
Sino-auricular node, 272
Skatol, 206
Skeleton, physiology of, 47
Skin, 472, 670
  nerve endings in, 670
  reflexes, 541
Sleep, 600
Smell, sense of, 677
Sodium glycocholate, 195
  taurocholate, 195
Spectroscope, 249
Speech, 658
Spermatozoa, 731
Spheno-palatine ganglion, 646
Sphygmograph, 367
Sphygmomanometer, 355
Spinal accessory nerve, 639
Spinal cord, 528
    encephalo-spinal conduction, 547
    functions of, 534
    nerve-cells, classification of, 530
    nerve-fibers of, 531
      classification of, 531
    redex actions of, 537, 541
    reflex irritability of, 539
    relation of spinal nerves to, 526
    segmentation of, 528
    spinal nerve roots, functions of, 527
    spino-encephalic conduction, 544
    structure of gray matter, 528
    structure of white matter, 531
    tracts of, 532
Spinal segments as conductor, 543
  as independent centers, 534
Spirometer, 407
Splanchnic nerves, 184, 202, 387, 649, 654
Spleen, 506
  functions of, 507
Stannius ligatures, 300
Stapes, 715
Starch, 7
  digestion of, 151, 190
Starvation, 128
Steapsin, 191
Stearin, 11
Stereognostic area, 586
Stomach, 165
  movements of, 179
  nerve mechanism of, 183
String galvanometer, 759
Suprarenal capsules, 500
Sweat-glands, 472
Sweat, influence of nerve system on production of, 472

Taste buds, 676
  nerve of, 675
  sense of, 675
Tawara's node, 273
Teeth, 141
Tegmentum, 555
Temperature of human body, 438
  sense, 673
Tendon reflexes, 542
Tension of gases in blood, 417
  tissues, 417
Tensor tympani muscle, 715
  functions of, 721
Thermogenesis, 441
Thermolysis, 448
Testicles, 730
Tetanus, 72
  experimental, 75
  pathologic, 75
  pharmacologic, 75
  physiologic, 74
Thoracic duct, 213
Thorax, 392
  dynamic condition of, 397
  mechanic movements of, 394
  static condition of, 395
Thyroid gland, 490
  effects of removal, 492
Tissue spaces, 201
Tongue, 676
Total carbon-dioxid exhaled, 422
  oxygen absorbed, 422
  respiratory exchange, 421
Touch, sense of, 670
Trachea, 389
Traube-Hering waves, 387
Trochlear nerve, 622
Trypsin, 191
Türck, column of, 532
Tympanum, 713

Upper air-passages, respiratory movements of, 404
Urea, 455
  seat of formation, 455
Ureter, 462

Uric acid, 457
Urination, 469
    nerve mechanism of, 470
Urine, 453
    composition of, 454
    mechanism of secretion, 462, 465
        influence of blood composition, 469
        influence of nerve system, 468
            of blood-pressure, 466
Uterus, 728

Vagina, 728
Vagus nerve, 634
    bathmotropic, 322
    chronotropic, 322
    dromotropic, 322
    influence on heart, 317
    inotropic, 322
    seat of action, 321
Valves of heart, 268–278
Vas deferens, 731
Vascular apparatus, 328
    application to vascular apparatus, 337
    hydrodynamic considerations, 332
    stream bed, 338
        nerve mechanism of, 376
Vaso-motor center, 382
    central stimulation, 383
    nerves, 377
    reflex stimulation, 387
    vaso-dilatator nerves, 379
Veins, 331
    structure and function, 331
Velocity of blood, 360
Venous circulation, 331
    pulse, 369
Vertebral column, 47
Vesiculæ seminales, 731
Villi, 218
    functions of, 219
Visceral muscle, 85
    functions of, 88
    properties of, 86
Viscosity of blood, 233
Vision, 679
    accommodation, 694
    astigmatism, 701
    binocular, 706
    color perception, 709
    functions of retina, 704
    hypermetropia, 700
    myopia, 700
    presbyopia, 699
Visual angle, 692
Vital capacity of lungs, 407
Vocal bands, 661
    sounds, 664
Voice and speech, 665
Volume pulse, 370
Volumes of air breathed, 407

Wallerian degeneration, 99
Wernicke's pupillary reaction, 621
White blood-corpuscles, 255
    function of, 259
    migration of, 373
    origin of, 258
    physiologic properties, 257
    varieties of, 258
Wrisberg, nerve of, 629

Yellow spot, 682

Zymogen, 152
    pepsinogen, 171
    ptyalogen, 152
    trypsinogen, 192

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